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Lewis A. Conner ----------Editor
Hugh McCulloch----------Associate Editor

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The American Heart Journal

VOL. IV OCTOBER, 1928 NO. 1

Original Communications

MYOCARDITIS*

B. J. CLAWSON, M.D.
MINNEAPOLIS, MINN.

IN HEARTS showing the different types of cardiac failure, areas of fibrosis of varying degrees may not infrequently be found. There is a difference of opinion concerning the origin of these fibrotic areas. Some observers consider them to be the result of inflammation, while others look upon a greater part of the fibrosis as a result of myocardial anemia following a narrowing of the coronary arteries.

Cardiac failure with essential hypertension, old valve defects, coronary sclerosis, coronary thrombosis, toxic myocardium, and syphilitic aortitis is commonly diagnosed acute or chronic myocarditis without regard to the pathological condition of the heart.

The purpose of this paper is to study the character, origin, frequency, extent, and result of the myocardial injuries manifested anatomically in the various forms of cardiac failure in order to determine whether clinically a diagnosis of acute or chronic myocarditis should be made.

In studying these hearts the term myocarditis is used only where an inflammatory process in the heart muscle is made evident by an exudative or proliferative cellular reaction.

MATERIAL

A detailed gross and microscopical study of the myocardium was made in 429 cases of cardiac failure. The following outline shows the usual conditions which result in cardiac failure and the number of cases studied:

	cases
A. Endocarditis	
1. Acute rheumatic	30
2. Recurrent rheumatic	20
3. Subacute bacterial	60
4. Old valve defects	68
5. Syphilitic aortitis, most cases of which show endocarditis	106
B. Adherent pericardium	2
C. Right ventricular hypertrophy and dilatation	4
D. Essential hypertension	139

*From the Department of Pathology, University of Minnesota, Minneapolis, Minn. Read in abstract before the American Heart Association at Minneapolis, June 12, 1928.

C.B. 12-28-28

Thirty-seven of the hypertensive hearts are in the group in which death occurred suddenly from a narrowing or thrombosis of the coronary arteries. On the average, about 75 per cent of all patients dying from coronary sclerosis have a high blood pressure, as indicated by the clinical history or by the size of the heart observed at necropsy. The non-hypertensive cases with coronary sclerosis show a condition in the myocardium similar in all respects to that found in the myocardium in the cases with high blood pressure, with the exception of hypertrophy.

The myocardium was examined for gross and microscopical evidences of inflammation and fibrosis. The extent of narrowing of the coronary arteries from intimal thickening was carefully noted, especially in the cases in which clinically there were symptoms of coronary disease. Five blocks from various places in the myocardium were studied in each case. Much attention was given to the type and degree of inflammation, whether it was exudative or proliferative in character, or arranged in localized areas to form abscesses or Aschoff bodies. Diffuse exudative or proliferative inflammation was also carefully looked for. The condition of the myocardium immediately surrounding the medium-sized blood vessels was carefully studied to determine whether or not peri-arterial scars were present. Such scars are commonly found in hearts in which there has been a previous rheumatic inflammation. It has been pointed out by various observers that the rheumatic inflammation generally occurs near, and often surrounding, blood vessels. When healed, the area about these vessels remains in the form of scars similar to those resulting from proliferative inflammation in heart valves or in any other part of the body.

The material studied in this paper can be placed in two groups. The first group includes the cases which result from inflammation, such as the various types of endocarditis (rheumatic, bacterial, and syphilitic) and the adherent pericardium. The second group includes the cases of cardiac failure following increased blood pressure, either systemic or pulmonary, and the cases where death resulted from a narrowing of the coronary arteries.

A detailed description of the myocardium in the various conditions associated with cardiac failure is given under the following headings:

Acute Rheumatic Endocarditis.—Death immediately associated with acute rheumatic fever is of infrequent occurrence and for that reason the study of the myocardium in a large series has not been made. It is evident, however, that this is one of the conditions in which acute myocarditis is found. Table I shows the type and frequency of inflammation in the 30 cases of acute rheumatic endocarditis which came to necropsy. It is seen that the Aschoff body is one of the outstanding evidences of inflammation. The Aschoff nodule is a localized area of inflammation mostly proliferative in character; but at times poly-

TABLE I

THE MYOCARDIUM IN ENDOCARDITIS

KIND	NO.	ASCHOFF BODIES		IRREGULAR PROLIFERATIVE INFLAMMATION		ABSCESSES		ACTIVE INFLAMMATION		PERIARTERIAL SCARS		TOTAL EVIDENCE OF INFLAMMATION, ACTIVE OR HEALED	
		NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Acute rheumatic	30	21	70	18	60	2	6.5	24	80	–	–	24	80
Recurrent rheumatic	20	12	60	12	60	–	–	13	65	–	–	13	65
Subacute bacterial	60	27	45	36	60	13	21.5	44	73.5	38	63.5	53	88.5
Old valve defect	68	9	13	14	20.5	0	0	15	22	36	53	36	53

morphonuclear leucocytes, lymphocytes, plasma cells, and eosinophiles in varying numbers are present. The anatomy of these nodules has been described by Aschoff,[1] Geipel,[2] Coombs,[3] Fraenkel[4] and others. By many these nodules are considered specific for the virus producing rheumatic fever. This, as is shown later in studying other types of cardiac disease, does not appear always to be the case. The Aschoff bodies in varying numbers and varieties are present in 21 (70 per cent) of the 30 cases of acute rheumatic endocarditis. Fraenkel,[4] one of the earliest observers of the Aschoff nodules, found them present in the myocardium in 17 (85 per cent) of 20 cases examined. Libman[5] found them in 18 (32 per cent) of 56 cases and Thayer[6] in 22 (88 per cent) of 25 cases.

In 18 (60 per cent) of the 30 cases studied in this paper there was an irregular proliferative inflammation with a cellular reaction similar to that found in the Aschoff nodule. This type of inflammation occurs as a rule in the interstitial tissues, as does the Aschoff body. Various forms of large, elongated, irregular mononuclear and multinucleated cells having vesicular nuclei and basophilic cytoplasm are found in this diffuse and irregularly arranged proliferative inflammation. Cellular exudates similar to those found in the Aschoff bodies are also commonly present.

Abscesses as a rule are rare in the myocardium in cases of acute rheumatic endocarditis. In one of the 7 cases studied, Geipel[2] found abscesses and considered their presence the result of a secondary infection with staphylococci, although he does not report detecting these organisms by either staining or cultural methods. Abscesses as well as Aschoff nodules in large numbers were present in 2 (6.5 per cent) of the 30 cases. These two cases were typical clinical and anatomical examples of acute rheumatic endocarditis with pericarditis.

Active inflammation indicated by Aschoff bodies, irregular proliferative inflammation, or abscesses was present in 24 (80 per cent) of the 30 cases of acute rheumatic endocarditis.

Myocarditis, acute in character, is of common occurrence in cases of acute rheumatic endocarditis. The myocarditis shows a great tendency to surround vessels. It is generally proliferative in character and may leave areas of myocardial fibrosis, the extent of which may be determined by studying the myocardium in cases of old valve defect. The acute myocarditis may be at times so extensive as to be considered a factor in bringing about myocardial failure, but it evidently is not of great importance in producing cardiac failure, since death so seldom occurs in acute rheumatic endocarditis. Death immediately associated with acute rheumatic fever comprises only about 2 per cent of the total cardiac failures.

Recurrent Rheumatic Endocarditis.—This group includes cases which have had repeated attacks of acute rheumatic endocarditis and at

necropsy show the verrucous rheumatic vegetations upon previously thickened valves.

The frequency of acute myocarditis in the 20 cases of recurrent rheumatic endocarditis in the series is shown in Table I. The types and character of inflammation are similar to those found in the cases of acute rheumatic endocarditis. Abscesses, however, are not found. Active inflammation, present in 13 (65 per cent) of the 20 cases, is slightly less frequent in the recurrent than in the acute rheumatic cases.

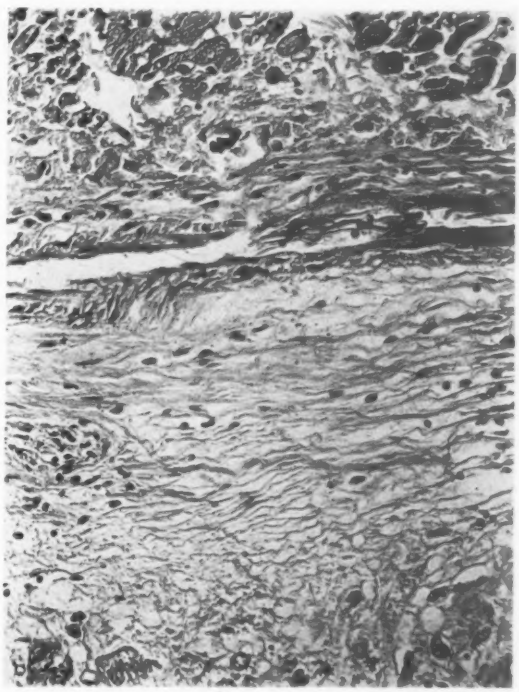

Fig. 1.—A peri-arterial scar showing the cellular remains of a proliferative inflammation.

Subacute Bacterial Endocarditis.—The frequency and character of active inflammation and its end-result, the scar, are shown in Table I. It is not the purpose of this paper to enter into a discussion of the etiology of rheumatic fever, yet it is of interest to observe the similarity of the type of reaction found in the myocardium in acute rheumatic endocarditis to that in subacute bacterial endocarditis and the relative frequency of this inflammation in both cases. It appears from Table I that the character of the inflammation found in the myocardium cannot be used absolutely as a means of differentiation between acute rheumatic endocarditis and subacute bacterial endocarditis.

In the 60 cases of subacute bacterial endocarditis in which the myocardium was studied, Aschoff nodules were present in varying numbers in 27 (45 per cent). Often they would not have been detected if several sections had not been carefully examined. Irregular proliferative inflammation was present in 36 (60 per cent).

One outstanding point to be noted in the myocardium in cases of subacute bacterial endocarditis is the high percentage of abscesses. They are found in 13 (21.5 per cent) of the 60 cases examined. The greater frequency of abscesses in subacute bacterial endocarditis than in other forms of endocarditis evidently results from the lodging in the myocardium of infected emboli from the valves.

Fig. 2.—A peri-arterial scar with part of an Aschoff nodule.

Active inflammation of the myocardium represented by one or more of the described types was present in 44 (73.5 per cent) of the 60 cases. This frequency compares well with that found in acute rheumatic endocarditis. The type of scar in the myocardium in subacute bacterial endocarditis is characteristic. It is located for the most part immediately around the medium- and small-sized blood vessels and is spoken of as peri-arterial fibrosis. In most cases cellular remains of proliferative inflammation can be seen (Fig. 1). It is not uncommon to find Aschoff nodules or parts of nodules within the scars (Fig. 2). The remaining cells of these nodules have laid down collagenous fibers.

The scar is obviously the result of rheumatic peri-arterial inflammation either in diffuse or nodular arrangement. Such scars never become severe but are large enough to indicate a previous peri-arterial infection. They differ from the scar associated with coronary disease in showing a more definite and immediate relation to the blood vessels and in most cases in showing some cellular proliferative or exudative reaction. These inflammatory scars are rarely seen in the myocardium in acute rheumatic endocarditis, since apparently the inflammation has not had time to form scars, but appears as active peri-arterial inflammation. The fate of the Aschoff nodule and the diffuse rheu-

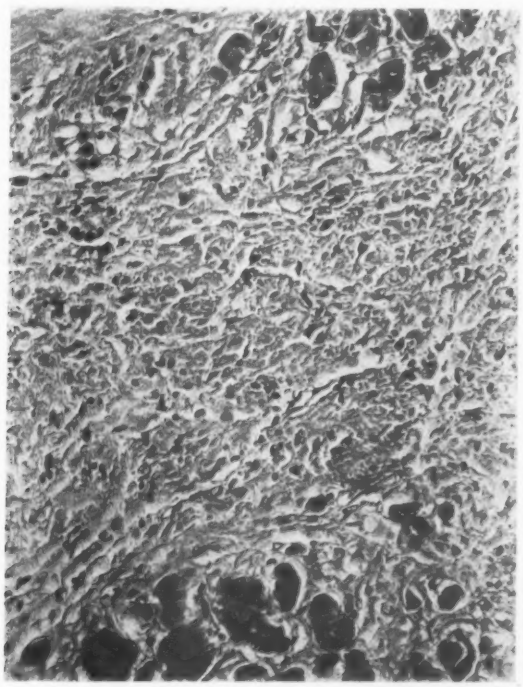

Fig. 3.—A scar from atrophy of muscle fibers with replacement by connective tissue.

matic proliferative inflammation upon healing is to form scars generally peri-arterial in arrangement and as a rule not very extensive.

The peri-arterial scar indicating a previous peri-arterial myocarditis is especially conspicuous in the myocardium in cases of subacute bacterial endocarditis. All transition stages may be seen from the active peri-arterial myocarditis, often containing Aschoff bodies, to the fully formed peri-arterial scars. These scars were found in 38 (63.5 per cent) of the 60 cases examined.

Evidence of inflammation, either active or healed, was found in 53 (88.5 per cent) of the 60 cases. It is to be noticed that myocarditis is even more frequent in subacute bacterial endocarditis than in acute

or recurrent rheumatic endocarditis. It seems reasonable that this should be so since an active infection is present over a longer period of time. Real chronic myocarditis is found in the myocardium in cases of subacute bacterial endocarditis in a higher percentage than in any other cardiac condition which we have observed. The injury to the myocardium in many cases of subacute bacterial endocarditis is to be considered a factor in the cardiac failure.

Old Valve Defects.—The frequency and types of myocardial inflammation in 68 cases where death resulted from old valve defects are shown in Table I. The Aschoff nodule was found 9 times (13 per cent). In 14 (20.5 per cent) there was irregular proliferative inflammation. Abscesses were not found in any. Active inflammation including all types was present in 15 (22 per cent). Peri-arterial scars, indicating a healed peri-arterial inflammation, were seen 36 times (53 per cent). It is to be noted that the scars are not as frequent as in the cases with subacute bacterial endocarditis. An active inflammation probably was not present over as long a period of time.

Evidence of inflammation, active or healed, was present in 36 (53 per cent) of the 68 cases. Except in one case the extent of this inflammation and fibrosis was slight and apparently had had little or no influence in bringing about the cardiac failure. The degree of coronary sclerosis was so slight, when present at all, that it appears evident that the myocardial fibrosis did not result from narrowing of the coronary arteries as it so commonly does in patients dying from coronary sclerosis.

In summarizing the facts concerning the injury found in the myocardium in the various forms of rheumatic and bacterial valvular diseases, it may be said that acute myocarditis is of common occurrence in acute rheumatic endocarditis (80 per cent), in recurrent rheumatic endocarditis (65 per cent), and in subacute bacterial endocarditis (73.5 per cent); but that it is most common in the acute rheumatic form. Acute myocarditis is only relatively frequent in cases of cardiac failure from old valve defects (22 per cent). Chronic myocarditis in the form of the peri-arterial scar occurs commonly in cases of subacute bacterial endocarditis (61.5 per cent) and in cases of old valve defects (53 per cent). Evidence of myocarditis, acute or chronic, is found more frequently in subacute bacterial endocarditis than in any other form of cardiac failure (88.5 per cent). The relative frequency of acute and chronic myocarditis in the above forms of endocarditis should be kept in mind in making clinical interpretations.

Adherent Pericardium.—The myocardium in cases in which death results from adherent pericardium shows practically the same condition as is found in the myocardium in old valve defects. Most cases of adherent pericardium also have defective valves. The cause in both

TABLE II

MYOCARDIUM IN HEARTS WITH SYPHILITIC AORTITIS (106 CASES)

GROUP / DEATH FROM	NO.	PER CENT	CORONARY SCLEROSIS						MYOCARDIAL FIBROSIS						PROLIFERATIVE INFLAMMATION	
			SEVERE		SLIGHT		NONE		SEVERE		SLIGHT		NONE			
			NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Aortic insufficiency	46	43.5	1	2	8	17.5	37	80.5	–	–	9	19.5	37	80.5	3	6.5
Closure of coronary orifices	25	23.5	–	–	3	12.0	22	88.0	–	–	2	8.0	23	92.0	4	16.0
Rupture of aortic aneurysm	35	33.0	–	–	–	–	35	100.0	–	–	–	–	35	100.0	4	11.5
Total	106		1	0.9	11	10.5	94	88.5	0	0	11	10.5	95	89.5	11	10.5

conditions is evidently a previous rheumatic infection. The degree of injury in the myocardium with an adherent pericardium, as indicated by anatomical change, is slight and evidently not the cause of the cardiac failure.

Syphilitic Aortitis.—Death from syphilitic aortitis represents about 10 per cent of all cardiac deaths. As in most other forms of valve defect, the chief change to be noted in the myocardium is hypertrophy. The myocardium was studied in 106 cases of syphilitic aortitis. Based upon the clinical course and the pathological conditions at necropsy these cases may be divided into three groups.

1. Aortic insufficiency, 46 cases (43.5 per cent).
2. Sudden death from closure of coronary orifices, 25 cases (23.5 per cent).
3. Rupture of aortic aneurysm, 35 cases (33.0 per cent).

In group I, where death results from aortic insufficiency, marked myocardial hypertrophy is noted. The condition of the coronary arteries and myocardium was studied in 46 cases of this group (Table II). Severe proximal coronary sclerosis was noted in one and slight proximal coronary sclerosis in 8. The coronary arteries showed evidence of senile sclerosis in but 9. Injury to the coronary arteries in syphilitic aortitis is unusual except at their orifices in the root of the aorta. Slight myocardial fibrosis of the atrophic type was present in 9 cases. By the atrophic type of myocardial fibrosis is meant a fraying out of the muscle fibers and a replacement with connective tissue (Fig. 3). In 37 cases (80.5 per cent) of this group no coronary sclerosis or atrophic myocardial changes were noted. In only 3 of the 46 cases (6.5 per cent) could small areas of proliferative inflammation be detected. These proliferative inflammatory areas were evidently due to syphilitic infection and were of so slight extent that it would seem they had little to do with the cardiac failure.

In Group II, where death resulted suddenly from narrowing of the coronary orifices, 25 cases were studied (Table II). Coronary sclerosis to a slight extent was found in only 3 of the 25. In the remaining 22 (88 per cent) the coronary arteries appeared normal except at their orifices in the aorta. Slight myocardial fibrosis of the atrophic type occurred in only 2 of the 25 cases. In 23 (92 per cent) there was no indication of myocardial injury following proximal coronary narrowing. In 4 (16 per cent) small areas of proliferative inflammation with lymphocytes were detected. In this group the myocardium in all but a few cases shows no anatomic change except the hypertrophy.

In Group III, or in the cases of syphilitic aortitis in which death resulted from a rupture of a syphilitic aortic aneurysm, 35 cases were studied (Table II). No coronary narrowing or myocardial fibrosis of

the atrophic type was found in any of these 35 hearts. Small areas of proliferative inflammation were found in 4 (11.5 per cent). As in the other groups the myocardium shows little anatomical change.

It seems evident that, even in a slight degree, myocarditis with syphilitic aortitis is rare and that death, except in a few cases with myocardial gummas, is seldom if ever due to a myocardial inflammatory condition or to scars resulting from inflammation.

Hypertensive Hearts.—This is the type of myocardial failure which is commonly diagnosed as due to chronic myocarditis by clinicians. On the basis of the manner in which death occurs, the 139 hypertensive hearts can be classed in four groups as follows:

1. Death with congestive failure, 78 cases (56.0 per cent).
2. Death from coronary sclerosis, 37 cases (26.5 per cent).
3. Death from cerebral hemorrhage, 16 cases (11.5 per cent).
4. Death from renal insufficiency, 8 cases (5.5 per cent).

Seventy-eight (56 per cent) of the 139 cases with hypertension are in the group having congestive heart failure (Table III). In none of these hearts is there any cellular proliferation or exudation except in those in which there are infarcts. The myocardial fibrosis bears a close relation to coronary sclerosis. There is coronary sclerosis in a severe degree in 12 (15.5 per cent) of the 78 cases, and severe myocardial fibrosis in 2 (2.5 per cent). There is slight coronary sclerosis in 54 (69 per cent) of this group and slight myocardial fibrosis in 35 (44.5 per cent). No narrowing of the coronaries is noted in 12 (15.5 per cent) and no myocardial fibrosis in 41 (52.5 per cent).

It should be observed that severe myocardial fibrosis is present in only 2.5 per cent of the group. In the remainder the fibrosis is slight or absent. It seems evident that the fibrosis is not due to inflammation and that, in a great majority of cases, the cause of the myocardial failure is some other factor than an inflammation or a fibrosis in the myocardium.

Thirty-seven (26.5 per cent) of the 139 cases with hypertension are in the group where death resulted from severe coronary sclerosis or thrombosis. Although there are many cases of death from coronary sclerosis in which there is no clinical history of a high blood pressure and in which there is no cardiac hypertrophy, only cases of coronary sclerosis with hypertension are included in this study. In hearts from cases where death occurred from coronary sclerosis without evidence of high blood pressure or cardiac hypertrophy, fibrosis is present as often and to as great an extent as in cases of coronary sclerosis with hypertension. Table III shows the involvement of the coronary arteries and the myocardium in the hypertensive cases with coronary sclerosis. Coronary thickening is present to a severe extent in all of

TABLE III

MYOCARDIUM IN HYPERTENSIVE HEARTS (139 CASES)

GROUP / DEATH FROM	NO.	PER CENT	CORONARY SCLEROSIS						MYOCARDIAL FIBROSIS					
			SEVERE		SLIGHT		NONE		SEVERE		SLIGHT		NONE	
			NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Congestive failure	78	56.0	12	15.5	54	69.0	12	15.5	2	2.5	35	44.5	41	52.5
Coronary sclerosis	37	26.5	37	100.0	–	–	–	–	18	48.5	17	46.0	2	5.5
Cerebral hemorrhage	16	11.5	6	37.5	8	50.0	2	12.5	–	–	6	37.5	10	62.5
Renal insufficiency	8	5.5	1	12.5	5	62.5	2	25.0	–	–	1	12.5	7	87.5
Total	139		56	40.5	67	48.0	16	11.5	20	14.5	59	42.5	60	43.0

the 37 cases. There is thrombosis in 27 (73 per cent). While myocardial fibrosis is found in all except 2 of the 37 hearts, it is severe in only 18 (48.5 per cent). The myocardium in this group shows a greater degree of injury than is found in hearts with congestive failure. This suggests the coronary narrowing as the cause of the fibrosis. It is evident that the fibrosis of the myocardium is of slight significance as a cause of cardiac failure since in more than half of the cases the fibrosis is slight or absent.

In Table III it is seen that 16 (11.5 per cent) of the 139 cases of hyperpiesia are in the group having a mild degree of cardiac decompensation and death from cerebral hemorrhage. Severe coronary sclerosis is present in 6 (37.5 per cent). Severe myocardial fibrosis is not noted. In 8 (50 per cent) of the 16 cases there is a slight degree of coronary sclerosis and there is a slight fibrosis of the myocardium in 6 (37.5 per cent). This fibrosis appears to have resulted from the coronary narrowing but is not responsible for the death, since death was due to cerebral hemorrhage.

In Table III it is seen that only 8 (5.5 per cent) of the 139 cases are in the group with mild cardiac decompensation where death resulted from renal insufficiency. In another series of 400 cases of hyperpiesia about 10 per cent are in this group. Coronary sclerosis is present in 6 of the 8 cases but it is severe in only one. Myocardial fibrosis is found in but one case and in this the fibrosis is slight.

A summary of the involvement of the coronary arteries and the myocardium in the 139 cardiac cases with hyperpiesia is given in Table III. Coronary sclerosis is present to a severe degree in 56 (40.5 per cent). Thirty-seven of these are the cases where death occurred suddenly from coronary narrowing. Severe myocardial fibrosis is noted in only 20 (14.5 per cent) of the 139 cases. Eighteen of these 20 cases are from the group dying from coronary sclerosis. Slight coronary sclerosis is found in 67 (48 per cent) of the entire group. There is slight myocardial fibrosis in 59 (42.5 per cent). It is to be emphasized that myocardial fibrosis to a severe extent occurs in only 14.5 per cent of the 139 cases, that no fibrosis is seen in 43 per cent, and that in the remaining 42.5 per cent the fibrosis is slight and of little or no significance.

The following facts are suggested from the study of the myocardium in these 139 cases of hyperpiesia: the fibrosis found in the myocardium is not inflammatory in origin, but apparently results from a myocardial anemia following narrowing of the coronary arteries. Fibrosis of the myocardium to a severe extent is present in only about 15 per cent of the cases, most of which are in the group where death resulted from the narrowing of the coronary arteries, and even in this group less than half show myocardial fibrosis of any significance. Fibrosis of the myocardium is of little importance in bring-

ing about myocardial failure in cases of hyperpiesia. Some factor or factors not manifested anatomically have the chief part in bringing about myocardial failure in hypertensive hearts and hearts with coronary sclerosis.

Right Ventricular Hypertrophy and Dilatation.—A small group of hearts fail following hypertrophy and dilatation of the right ventricle resulting from increased pulmonary pressure. This may occur in such conditions as chronic bronchial asthma, chronic emphysema, chronic bronchiectasis, and in the so-called Ayerza's disease. Four of the 429 cases studied in this paper are in this group. Slight fibrosis is noted in all of the 4 hearts. This fibrosis appears to have resulted from an inflammatory condition since Aschoff bodies or irregular areas of proliferation are found in all. The fibrosis is present in the left ventricle while the hypertrophy is in the right ventricle. This suggests that there is no causal relationship between the increased pressure and the fibrosis. It also indicates that the slight amount of fibrosis probably has nothing to do with bringing about cardiac failure.

DISCUSSION

Two anatomical types of myocardial injury are noted in many of these 429 cases of cardiac failure. First, there are the inflammatory injuries which are shown as exudative or proliferative changes either in localized areas or scattered diffusely throughout the heart in the interstitial tissues. The inflammation shows a great tendency to be arranged about blood vessels and upon healing, to leave scars with a periarterial arrangement. The second type of myocardial injury is the myocardial fibrosis without any evidence of an association with inflammation. These scars appear as areas of atrophy of the muscle fibers with a replacement by connective tissue. This second form of myocardial scar is a definite result of coronary sclerosis of the senile type.

The inflammatory type of myocardial injury is common in all forms of rheumatic and bacterial valvular injuries, but it is rare in the myocardium in syphilitic aortitis. It occurs seldom or not at all in the myocardium in cases where death results from essential hypertension or from coronary sclerosis. The atrophic scars are rarely found in cases of cardiac failure except in the groups having hypertension and coronary sclerosis. Myocardial fibrosis of either the inflammatory or the atrophic type is seldom present to a severe extent except in the group where death results from coronary sclerosis. Here it is found in only a relatively small percentage of cases.

The result of the active myocarditis probably is somewhat of a factor in bringing about cardiac failure, but the atrophic form of fibrosis, even in its severe degree, does not seem to be of much importance as a cause of death.

It is doubtful whether the clinical diagnosis of either acute or chronic myocarditis should be made, even though such a condition commonly exists in association with a valvulitis. It is certain that what is called chronic myocarditis clinically in chronic heart failure without valvular injury is not an inflammatory condition and in most cases it is not any other condition in the myocardium showing an anatomical basis for the failure.

SUMMARY

1. Myocarditis, acute or chronic, arranged diffusely or in localized areas as Aschoff nodules or abscesses, is a common condition in the myocardium in acute and recurrent rheumatic endocarditis, in subacute bacterial endocarditis, and in old valve defects.

2. The peri-arterial scars appear to be the result of a previous bacterial infection and are frequently found in the myocardium in cases of subacute bacterial endocarditis and old valve defects.

3. Proliferative or exudative inflammation is rare in the myocardium in cases of syphilitic aortitis.

4. Scars resulting from atrophy of muscle with replacement by connective tissue following a narrowing of coronary arteries seldom occur except in the myocardium in cases of hypertension and coronary sclerosis.

5. The extent of myocardial injury as shown by anatomical changes rarely appears to be sufficient to bring about cardiac failure.

6. The conditions usually diagnosed acute or chronic myocarditis clinically cannot be demonstrated to be inflammatory processes and in most cases anatomical injuries are not seen.

7. So-called myocarditis is usually a condition of the myocardium, probably fatigue, which is not manifested anatomically.

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(*For discussion, see page* 117.)

THE RELATION OF THE ADRENALS TO THE CIRCULATORY COLLAPSE OF DIPHTHERIA*

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IN EARLIER papers from this laboratory it was shown that one of the most important factors concerned in the circulatory collapse which occurs in diphtheria is a greater or less degree of paralysis of the splanchnic nerves. This paralysis allows the abdominal vessels to relax, and these, acting as a reservoir, lessen the amount of blood to be returned to the heart and bring about a "distributive oligemia." In addition to this lack of circulating blood, there is in severe cases of diphtheria a heart profoundly affected by the toxin—a toxic parenchymatous myocarditis—and this must affect the circulation deleteriously. However, it is still an open question as to just how large a part the myocarditis plays in the circulatory failure. Indeed it has been abundantly proved that such hearts, although markedly pathological, will still maintain a satisfactory circulation provided they are supplied with sufficient blood. The vasomotor center and the muscular walls of the vessels appear to react normally. However, other structures which might be concerned in the circulatory embarrassment and which deserve careful study in this connection are the adrenal glands. Abramow,[1] one of the earlier investigators upon the reaction of the adrenals to diphtheria intoxication, described the changes produced in the glands by the toxin when it is given either in doses causing death in a comparatively short time or merely in sublethal doses. While with the small doses he believed there was evidence of stimulation of those glands, with the large doses there was evident epinephrin poverty and he ascribes the circulatory disturbance with resulting failure of the heart largely to this factor. One of the more recent writers on the subject (Harding[2]) says that in diphtheria the adrenals show a hyperchromatism with increased staining of the nuclei followed by hypochromatism progressing in places to dissolution of the nuclei and breaking down of the cells. However, it may be said that the significance of these changes is not completely understood nor the part which they may play in causing a disturbance of the function of these glands. In addition, it is not at all unlikely that some of the changes in the adrenals which have been described are not specific for diphtheria at all, as they may be present in any severe acute infection or may even be due to post-mortem processes.

The epinephrin content of the glands in diphtheria was investigated by Ehrmann,[3] who used the isolated frog's eye method of assay.

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He reported that even in severe cases of diphtheria intoxication with marked pathological changes in the glands there was still epinephrin present in the blood and that it might even be present in an increased amount. It must be pointed out, however, that the method of assay utilized by Ehrmann has not been found to be satisfactory by many of the other workers and therefore his conclusions cannot be accepted at their face value. Elliott[4] in the same year reported that the staining properties of the cells of the adrenals when treated with mixtures containing chromic acid were much diminished after poisoning with the toxin and that the intensity of the stain corresponded with the amount of epinephrin which could be extracted from the gland. In a later paper[5] he states that the amount of epinephrin was much diminished in the adrenals of cats which had died of diphtheria and that the amount was decreased to a greater extent on the side with intact splanchnics as compared with the side on which the nerve had been cut. For instance, with an average yield of 0.25 mg. of epinephrin from a normal gland he obtained from the adrenal of a diphtheritic animal on the side with the intact nerve only 0.02 mg. while on the side with the nerve cut he found amounts varying from 0.15 mg. to 0.22 mg. The difference between the two sides was very striking in every case. Elliott concluded that the action of the toxin was not a direct one upon the gland but was due to some action which reached the glands by way of the splanchnics. He did not think that the exhaustion of the epinephrin was a primary cause of death. Ritchie and Bruce[6] found, much like Abramow, that in the more acute type of diphtheria in guinea pigs there was a considerable diminution in epinephrin while in more protracted cases there was complete exhaustion. So also Broberg[7] reported changes in the adrenals in protracted diphtheria but stated that they were no more than could be explained by the general cachexia. Lucksch[8] has also called attention to the fact that in this intoxication the epinephrin may be partly or wholly lost. The adrenals of some guinea pigs used by him were entirely inactive in so far as epinephrin was concerned, and in a dog which died after four days' illness he found no epinephrin. Also in children dead of diphtheria he found a diminished epinephrin content and he believes that such a change may be important in determining the course of the illness of the individual. More recently Hartman and Macdonald[9] reported that they were unable to demonstrate any increase in epinephrin in the blood of cats following the injection of diphtheria toxin. An examination of the glands by staining methods showed that at times the medulla appeared to be depleted but usually epinephrin was present in patches or in limited groups of cells. Finally Molinelli[10] has shown that in dogs and rats which have been injected with diphtheria toxin the weight of the adrenals is not increased. They may possess a normal aspect or may appear congested, but the amount of

epinephrin contained is in general diminished. He says also that the amount of epinephrin in the blood obtained from the suprarenal vein is also markedly lessened.

It will be seen by these brief references to the literature that most workers find a lessened amount of epinephrin in the adrenals of diphtheritic animals but it will also be noted that most of the reports are based upon impressions gained by a study of the intensity of staining reactions rather than upon definite estimations of the amount of the alkaloid which could be extracted from the glands. Accordingly, in connection with our studies upon the causes of the circulatory collapse in diphtheria, we have also investigated the epinephrin content of the adrenals in an effort to shed further light upon the question.

In the first place it was necessary to establish a normal epinephrin content for dogs as most of the figures which are available in the literature were obtained from animals which had been used in laboratory experimental work and which, therefore, had been subjected to various operative procedures in addition to a more or less prolonged anesthesia. Accordingly, we secured our normal controls from dogs immediately after anesthesia was complete, the anesthetic consisting of a subcutaneous injection of morphine (75 mg.) followed by urethane (1.5 gr. per kg.) given by means of a stomach tube. These same animals from which the adrenals had been removed were then used for the assay of both the normal and the diphtheritic glands; in many cases, therefore, the assay of the normal glands was carried out upon the same animal from which they had been removed.

We secured the diphtheritic glands from dogs immediately after death from the effects of the toxin. The epinephrin was extracted and then by means of the blood pressure method the amount of epinephrin in the solution was assayed by comparing it with a standard solution of epinephrin (Metz). The method of extracting the epinephrin from the glands was as follows, and was essentially that described by Folin, Cannon and Denis.[11]

After the glands had been removed from either the normal animal or from the animal dead from diphtheria, they were carefully separated from the surrounding fat and connective tissue, weighed, cut into small pieces and then ground in an agate mortar with N/10 hydrochloric acid. The mixture was placed in an Erlenmeyer flask and enough of the acid added to make 7.5 c.c. for each gram of gland. Three times as much water was then added and the mixture boiled. To this was added 10 per cent sodium acetate, 5 c.c. for each 15 c.c. of HCl, and the mixture brought to the boiling point again. It was then filtered and transferred to a volumetric flask (50 c.c. for each gram of gland) and filled to the mark. The standard solution was prepared from the Metz synthetic epinephrin by adding sufficient N/10 HCl to the alkaloid in water to bring it into solution and then diluting it with water to the desired strength, 1:1000. This solution was further diluted for use. The technic of the biological assay is well known. The dog being fully anesthetized, cannulas are inserted in the trachea for artificial respiration, in the carotid for the blood pressure record, and in the femoral veins for

the injection of the solutions. The vagi are cut and artificial respiration instituted. The two solutions—the standard and the unknown—are now injected in appropriate doses until a suitable comparison of strengths is found from which the epinephrin content of the unknown solution can be calculated.

The results obtained from the normal dogs are as follows:

Dog	*Weight*	*Weight of adrenals in milligrams*	*Total epinephrin in milligrams*	*Epinephrin per gram of gland*
1	11 Kg.	1250	1.74	1.39
2	6 Kg.	1025	1.10	1.07
3	9 Kg.	1100	1.15	1.05

These figures show in general a reasonable agreement with the figures usually given for the amount of epinephrin in the glands of the normal dog, viz., 0.1 per cent of the moist weight.

In considering the results obtained from the diphtheritic dogs, it is important to have information concerning the history of the disease in the individual animal in order that a proper comparison may be made with the conditions as found in the human subject. The dose of toxin must not be too large or the course of the disease will be so brief as to make a comparison impossible. Accordingly a history in briefest terms of each animal is given herewith.

Dog 1 D Weight 10 Kg.
12/2/26 Toxin 0.002 c.c. subcutaneously.
12/4/26 Toxin 0.002 c.c. subcutaneously.
12/6/26 Toxin 0.0015 c.c. subcutaneously.
12/7/26 Dog quiet—not eating.
12/8/26
9 A.M. Deeply apathetic—bloody vomitus and movements.
10 A.M. Stopped breathing. Artificial respiration, 10 per cent glucose intravenously.
Duration of intoxication—6 days.

Dog 2 D Weight 9 Kg.
2/21/27 Toxin 0.007 c.c. subcutaneously.
2/23/27 Very quiet, apathetic.
2/24/27 Toxin 0.01 c.c. Dog apathetic.
2/25/27 Dying, operated. Duration of intoxication—4 days.

Dog 3 D Weight 9.5 Kg.
2/21/27 Toxin 0.005 c.c. subcutaneously.
2/24/27 Toxin 0.003 c.c. subcutaneously.
2/25/27 Toxin 0.008 c.c. subcutaneously.
3/ 2/27 Quiet. Toxin 0.002 c.c. subcutaneously.
3/ 3/27 Dying. Operated.
Duration of intoxication—10 days.

Dog 4 D Weight 13.5 Kg.
2/28/27 Toxin 0.01 c.c. subcutaneously.
3/ 1/27 Inactive.
3/ 2/27 Toxin 0.01 c.c. subcutaneously.
3/ 5/27 Toxin 0.01 c.c. subcutaneously.
3/ 7/27 Dying. 3 P.M. operated.
Duration of intoxication—7 days.

The estimation of the epinephrin in the diphtheritic dogs, histories of which are given above, is as follows:

Dog	*Weight*	*Weight of adrenals in milligrams*	*Epinephrin in milligrams*	*Epinephrin per gram of gland*
1 D	10.0	1840	0.30	0.16
2 D	9.0	1800	1.25	0.69
3 D	9.5	1450	1.05	0.73
4 D	13.5	1725	1.05	0.61

These figures giving the epinephrin content of the adrenals in animals dying of diphtheria confirm the findings of Lucksch, Elliott and the others who report a lowering in epinephrin content in the glands in this disease, but what importance this diminution has in the life of the animal is not so easy to answer. In the first place the action probably is not specific for diphtheria. Lucksch, in particular, has shown that in many diseases, especially in tuberculosis, the epinephrin content of the glands may be lowered. It is not unlikely that Broberg is right when he says that the change may be explained by the general cachexia. It is certainly true that the factor of cachexia may play a rôle in the results obtained in the animals. Our dogs all showed symptoms of an acute illness, being very quiet on the day following the injection, eating and drinking little or nothing, and finally toward the end being apathetic and in some cases comatose. On the other hand, it would certainly seem probable that a diminution of epinephrin in the glands to perhaps 20 per cent of the normal amount or even as reported by some workers to a total absence of the alkaloid, could not help but be of importance in the expectancy of life of the individual. However, it is probably not a sudden exhaustion of the epinephrin which takes place. All the evidence is that it is a gradual affair extending over days while the typical circulatory collapse in diphtheria is an acute phenomenon—a matter of an hour or two—making it appear most likely that the adrenal exhaustion is not an important factor in the collapse but is merely an associated phenomenon.

SUMMARY

In diphtheria there is a marked diminution in the amount of epinephrin in the adrenal glands. This decrease in epinephrin is probably not the cause of the circulatory collapse.

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PAROXYSMAL VENTRICULAR TACHYCARDIA WITH ALTERNATING COMPLEXES DUE TO DIGITALIS INTOXICATION*

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IN THE past few years a considerable number of examples of paroxysmal ventricular tachycardia have been reported[1, 2, 3] and several authors have commented upon the probable relationship of the tachycardia to the administration of digitalis; Reid[4] particularly has emphasized the close association between the abnormal mechanism and preceding large doses of the drug. That the relationship is not an invariable one is clear, for in many of the recorded cases digitalis had not been given during the preceding days or weeks.[3] In 1922, Schwensen[5] published an extraordinary electrocardiogram displaying regular alternation of upward and downward ventricular deflections at a rate of 180 per minute; it was obtained from a patient whose electrocardiograms before and after the unusual mechanism showed auricular fibrillation. This was the first published example of the alternating type of ventricular tachycardia in the human being; similar curves were recorded in 1923 by Felberbaum,[6] in 1924 by Reid,[4] and two in 1925 by Luten.[7] In all five cases auricular fibrillation had been present before the development of the unusual ventricular tachycardia, and in three of them it was present after the tachycardia ceased; all of the patients had received digitalis in large doses, and the unusual mechanism was regarded in each instance as probably due to the administration of that drug. Reid's case differs from the others in one important respect, in that the alternation in direction of the ventricular complexes was present for only a few cycles about thirty seconds before the death of the patient, and immediately preceded the onset of ventricular fibrillation.

In each of the four reports mentioned above, the origin of the tachycardia is briefly discussed, each author recognizing that there are two possible explanations of the unusual rhythm. One is that there is a single focus, situated probably in the A-V node or in the A-V bundle above its bifurcation, sending out rhythmic impulses which travel alternately along the right and left branches of the bundle. This explanation assumes that the branch which has just transmitted an impulse is partially or wholly refractory to the next succeeding one; it is further assumed (Luten) that digitalis may be responsible for such an interference with bundle-branch conduction.

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The alternative explanation is that there are two foci sending out impulses, one in either ventricle, and that the tachycardia is composed of a rapid succession of ectopic beats arising alternately in right and left ventricles. In none of the reported cases has it been possible definitely to decide which type of mechanism was responsible.

The following five cases are reported partly because they represent a considerable addition to the small number of similar cases now on record, but chiefly because the electrocardiograms from several of them appear to throw light upon the nature of the mechanism involved, and because they provide additional evidence tending to show that digitalis is responsible for the condition. The present communication is concerned only with those instances of paroxysmal tachycardia in which there is constant alternation of upward and downward ventricular complexes at a rate usually exceeding 150 per minute. The essential facts of the histories will be presented briefly, and the important features of the electrocardiograms discussed subsequently.

CLINICAL REPORTS

CASE 1.—An Irish teamster, fifty-nine years of age, entered the hospital on January 23, complaining of shortness of breath, cough, and swelling of the legs. He stated that dyspnea had first become troublesome about four or five weeks previously and that orthopnea and swelling of the feet had been noted several days later. All symptoms increased rapidly; swelling of arms and hands was first observed two days before he came to the hospital. The previous history was irrelevant.

Physical examination at the time of admission showed orthopnea, urgent dyspnea, deep purplish cyanosis of lips, ears, and nail-beds of fingers, conspicuous engorgement of the neck veins, and well-marked nodding of the head. There was frequent unproductive cough. There were signs of fluid in both pleural cavities below the angles of the scapulae. The heart was considerably enlarged, the apex impulse being in the sixth left intercostal space in the anterior axillary line; the right margin of percussion dullness in the fourth right intercostal space was 4 cm. to the right of the median line. The auscultatory signs were those of stenosis and insufficiency of the mitral and aortic valves. The rhythm was regular, the rate 136 per minute. The liver edge was felt 8 cm. below the costal border in the right mammillary line; the tip of the spleen was just palpable. There was great edema of the subcutaneous tissues from the level of the umbilicus downward. The peripheral arteries were hard and tortuous. The blood pressure ranged from 115 to 130 mm. Hg. systolic, and 88 to 100 mm. diastolic.

The Wassermann reaction on the blood serum was negative. A seven-foot x-ray film of the heart showed considerable enlargement. Other laboratory data were not of importance.

Course and Treatment.—The patient was admitted at noon on Jan. 23. His weight was 133 pounds. Digitalis in the form of the powdered leaf was administered as follows: 0.6 gm. at 1 P.M., 0.4 gm. at 4 P.M., and 0.4 gm. at 8 P.M. on the twenty-third; 0.2 gm. at 8 A.M. and at noon on the twenty-fourth; a total of 1.8 gm. in twenty-four hours. On the morning of the twenty-fourth, a pleural friction rub was detected in the right axilla; several hours later the heart rate was found to be 160 per minute and apparently regular. An electrocardiogram

was taken and revealed the mechanism illustrated in Fig. 1. The tachycardia continued without interruption, so far as is known, throughout the remainder of the day and the night. On the following day (Jan. 25) there were clear signs of pulmonary infarction, but no fever. Throughout the day there were paroxysms of tachycardia, lasting from several minutes to several hours; the rate during these periods was usually very near 150 per minute, while between the paroxysms the rate was approximately 100 per minute. Electrocardiograms showed that the tachycardia was always of the same type, but there were minor variations in the size of the ventricular deflections during different paroxysms (Fig. 2). On the twenty-sixth, paroxysms of tachycardia were infrequent, but the pulmonary condition had extended and the patient seemed worse. During the next two days no paroxysms of tachycardia were detected by auscultation or in electrocardiograms, but the temperature rose steadily, the respirations increased in rate, signs of bronchopneumonia became widespread, and the patient died at noon on Jan. 28.

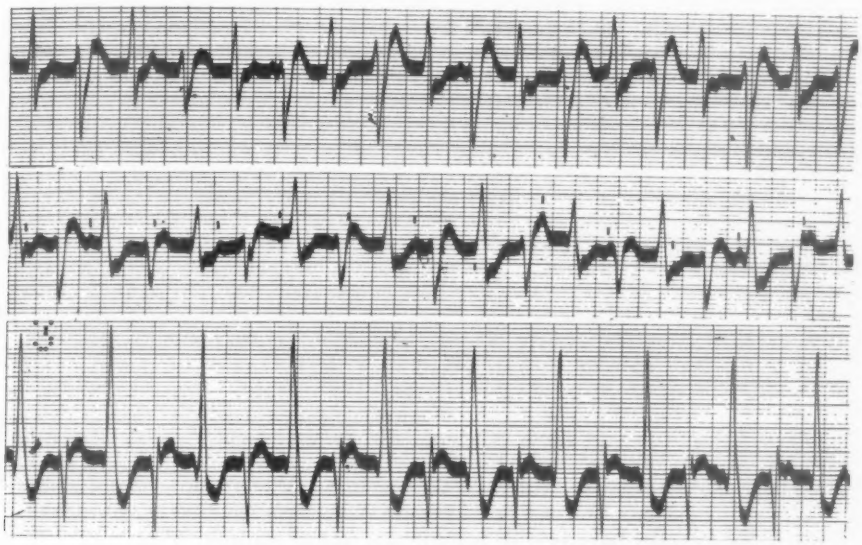

Fig. 1.—Case 1. Leads I, II, and III. Record obtained on Jan. 24. The auricular rate is 102.85 and the ventricular rate 146.9 per minute. The ventricular rhythm is slightly but definitely irregular in all leads. In Lead II, auricular waves are marked by small vertical lines. Notice the minor variations in form of ventricular deflections. (In this and all subsequent electrocardiograms distances between abscissae represent 10^{-4} volts, and time is in fifths of a second. Figures are full size except when otherwise stated. In many instances the stated rate has been calculated from long strips of film rather than from the published figure.) (x ⅔)

Autopsy.—There were signs of general passive congestion; there was free fluid in the pleural cavities and in the peritoneal cavity, and edema of the subcutaneous tissues. The lungs showed multiple areas of infarction. The liver extended 6 cm. below the costal border. The heart was greatly enlarged; it weighed 850 gm. There was an area of fresh fibrinous pericarditis near the apex of the left ventricle, about 4 cm. in diameter. The ventricular cavities were very large, especially the left. The wall of the right ventricle averaged 5 mm. in thickness, that of the left, 18 mm. There was a mural thrombus in the right auricular appendage. On the inner surface of the left ventricle near its apex, the location corresponding to the area of pericarditis, there was a thrombus firmly adherent to the wall, and undergoing organization. On section it was found to be hollow, the center having become necrotic. The ventricular wall beneath the thrombus was approximately

one-third the thickness of the wall elsewhere; its outer half was composed of dense fibrous tissue and its inner half of dull, lusterless, necrotic-looking muscle. A thrombus quite similar in appearance, but apparently more recent, was attached to the interventricular septum at the apex of the right ventricle. The tricuspid and pulmonary valves were normal in appearance. The mitral orifice was narrowed; the valve leaflets were thickened along the line of closure and showed many small irregular vegetations. The papillary muscles were greatly thickened and slightly flattened. The aortic valve cusps were thickened, sclerotic and adherent, with extreme calcification. The valve opening was reduced to a mere slit. The orifices

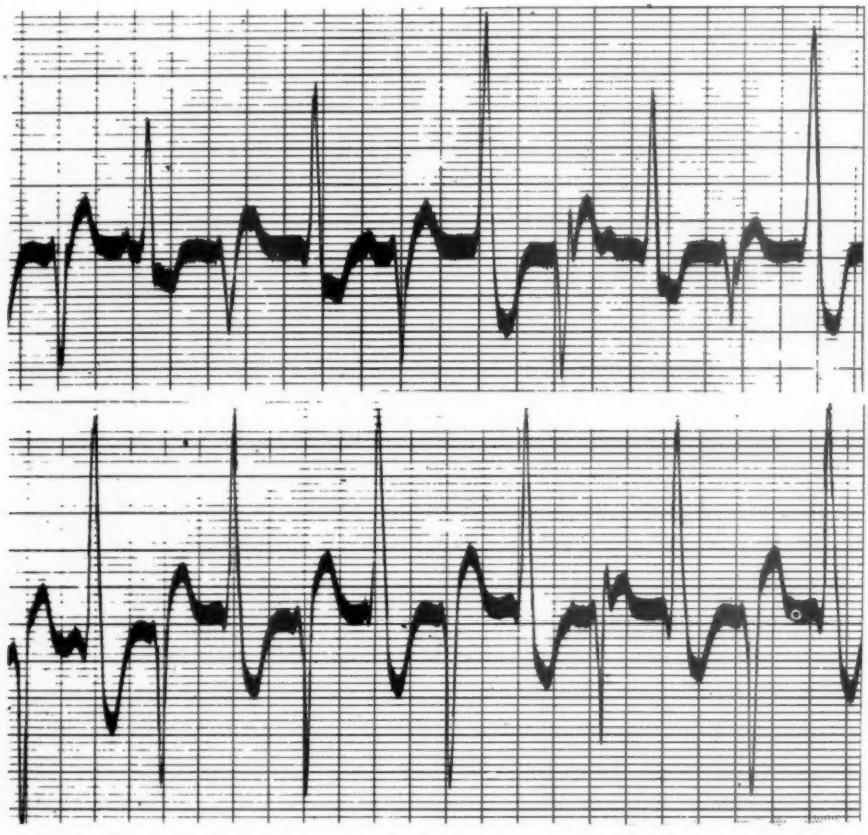

Fig. 2.—Case 1. Upper curve, Lead III, Jan. 24. Auricular rate, 93.7, ventricular rate, 138.46 per minute. Lower curve, Lead III, Jan. 25. Auricular rate not determined, ventricular rate 145.4 per minute. Notice especially the differences in size and shape of ventricular complexes.

of the coronary arteries were patent, and no closure of a vessel could be demonstrated by dissection or by stereoscopic roentgenograms taken after injection of the coronary vessels with barium gelatine.

Microscopic examination of sections from the heart showed an extreme degree of hypertrophy of the muscle fibers, with widespread fibrosis, especially about the blood vessels. A section through the thrombus in the left ventricle showed the picture of organization, with many fibroblasts and small capillaries; in places, endothelium could be seen growing over the surface of the thrombus. There was necrosis of the muscle fibers beneath the thrombus, with fibrosis in the outer

portion of the ventricular wall. Microscopic study of the vegetations on the mitral valve revealed them as dense, acellular connective tissue.

The anatomical diagnosis was: healed mitral endocarditis, healed and calcified aortic endocarditis with advanced stenosis, diffuse fibrosis of myocardium, organizing mural thrombi in ventricles, organizing pericarditis, cardiac hypertrophy and dilatation, chronic passive congestion of the viscera with general anasarca, pulmonary infarcts.

Electrocardiograms: Electrocardiograms were obtained at frequent intervals during the four days beginning with Jan. 24; several of them are reproduced in Figs. 1 to 4. Fig. 1 is taken from the first record secured on Jan. 24; it shows the type of tachycardia, with regular alternation in the direction of the ventricular complexes, which forms the subject of this paper. Numerous curves depicting this type of mechanism were secured during this and the two following days; some of

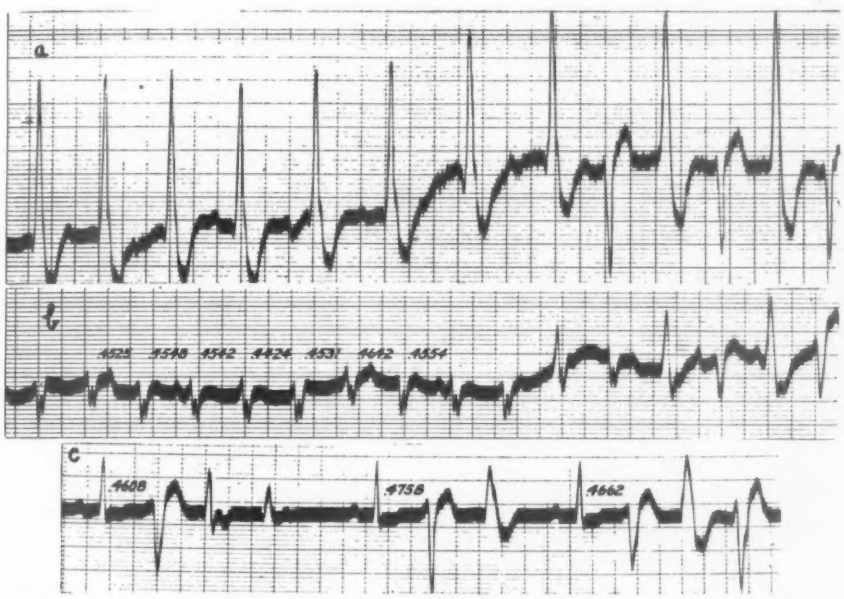

Fig. 3.—Case 1. *a*, Lead III, Jan. 25; *b*, Lead II, Jan. 24. These show the change from a tachycardia composed of precisely similar complexes to one in which there is regular alternation in direction of successive deflections. Auricular waves are distinct throughout *b*. *c*, Lead I, Jan. 26. Three normal beats, each followed after a similar interval by a group of ectopic ventricular beats, the last of which is probably the beginning of a paroxysm. Auricular waves are distinct and regular. (x $\frac{2}{3}$)

them were precisely like those of Fig. 1, and several showed slight differences in the size or configuration of the ventricular deflections, especially in Lead III. In the first two leads of Fig. 1 many auricular waves can be identified with certainty; these, as well as the position of those which are buried in the ventricular complexes, have been marked in Lead II, by placing opposite each of them a small vertical line. It is found that the auricular rhythm is perfectly regular and the rate 102.85 per minute, while the ventricular rate, measured over the same portion of film, is 146.9 per minute. Auricular waves are present in only two places in Lead III, toward the end.

Fig. 2, containing two portions of Lead III from electrocardiograms taken on different days, illustrates the minor variations in size and form of the ventricular complexes already mentioned. The upper curve of this figure was inserted because

it represents the lowest rate observed in any records from this patient, and also displays auricular waves more clearly than any other similar lead. The rate of the auricles is 93.7, that of the ventricles 136.46, per minute.

Fig. 3, *a* is a portion of Lead III from a record secured on Jan. 25; *b* is a portion of Lead II from a record obtained on Jan. 24, and *c* is a strip of Lead I from one of the curves of Jan. 26. The change from an undirectional paroxysm to one in which there is alternation in direction of the ventricular deflections is clearly shown in *a* and *b*. The latter portion of the curve in *a* is so distorted by extrinsic current as to permit no statement about the presence of auricular waves, but such waves can be clearly seen in *b*, occurring regularly and at a rate distinctly slower than that of the ventricles. In *c* there are shown three normal ventricular complexes, each preceded at a normal interval by an auricular summit. Each of the first two complexes is followed by a group of ectopic ventricular beats; the third is followed by three such beats which presumably represent the beginning of

Fig. 4.—Case 1. Three usual leads; I and II taken on Jan. 25, III on Jan. 26. The A-V conduction time is prolonged in all leads, but more in the curve of Jan. 25. Notice especially the direction of the ventricular complexes in Leads I and III.

a paroxysm, although this cannot be asserted with great confidence. The intervals separating the normal beats from the ectopic beats that follow are of almost identical length.

Fig. 4 represents the normal type of ventricular complexes for this patient. Leads I and II are from a record taken on Jan. 25; Lead III from one taken on the following day. The A-V conduction interval is prolonged in all leads, but less in Lead III than in Leads I and II; the interval is steadily approaching normal.

Comment.—The course of events in this patient seems clear. A man with advaced congestive heart failure and normal cardiac mechanism received an amount of digitalis considerably greater than that necessary for complete therapeutic effects, as gauged by his body weight. Just before the last fractional dose was given, it was found that the

normal cardiac mechanism had changed to one in which the ventricles were beating much more rapidly than the auricles, and electrocardiograms showed constant alternation in the direction of the ventricular deflections. This abnormal mechanism prevailed, so far as could be ascertained by frequent observation, for about twenty hours before the normal mechanism was restored. When the normal sequence of chamber contraction was resumed, the A-V conduction time was prolonged; partial heart-block was present. During this day (Jan. 25) paroxysms similar in nature to the original one, but of relatively brief duration, occurred many times; on the following day they occurred less frequently and were of shorter duration. The A-V conduction time, although still prolonged beyond the normal, was shorter than on the preceding day. The regular rhythm between the paroxysms was frequently interrupted by ectopic ventricular beats, occurring singly or in groups of two or three. On Jan. 27 neither paroxysms of tachycardia nor ectopic ventricular beats were detected, but the P-R interval was still slightly more than 0.2 second. On the morning of the twenty-eighth, four hours before the patient's death, the electrocardiogram showed normal mechanism.

Apart from the nature of the mechanism responsible for the curious alternating ventricular tachycardia, the point of chief interest and importance is the steady decrease in the length and frequency of the paroxysms of tachycardia until they were replaced by ectopic beats, which themselves became rapidly less frequent and disappeared completely. Coincident with this change in the abnormal mechanism, there was a similar change in the length of A-V conduction time; considerably prolonged at first, it became constantly shorter and, after three days, was within normal limits. There was thus a perfect, orderly transition from abnormal to normal through a series of defined stages each of which represented a less advanced disturbance than the preceding one. If the progression had been from normal to abnormal, each day revealing a disturbance of higher grade, there would probably be little hesitation in accepting it as evidence of increasing digitalis effects upon the heart. There is equally good reason for believing that the events as pictured represent steadily decreasing digitalis effects, coincident with the excretion of the drug from the body.

CASE 2.—A negro woman, fifty-three years of age, was admitted to the hospital on March 25 because of difficulty in breathing and swelling of the extremities. Eleven months earlier she had been troubled by headaches, dizziness, and blurring of vision, and at that time she was found to have hypertension. Four months before entry, she was said to have had severe "cardiac asthma"; one month later she entered a hospital because of increasing dyspnea and edema. Her subsequent history was one of steadily increasing congestive heart failure. The past history was irrelevant.

Examination revealed orthopnea, dyspnea, and moderate cyanosis of the mucous membranes. There was but slight fullness of the neck veins. The heart was considerably enlarged, the rhythm regular, the rate 120 per minute. There was a systolic murmur over the lower precordium. Signs of congestion were present over the bases of the lungs, the edge of the liver was 10 cm. below the costal margin in the right midclavicular line, and there was evidence of a moderate amount of free fluid in the abdomen. There was great edema of the subcutaneous tissues below the level of the umbilicus. There was moderate thickening of the peripheral arteries; the blood pressure was 160 mm. Hg. systolic, 100 mm. diastolic; subsequently it varied between 125 and 160 mm. systolic, 90 and 100 mm. diastolic. The blood Wassermann reaction was negative.

Course and Treatment.—The patient's weight was 161 pounds; later, when edema was no longer present, it was 133 pounds. She received no digitalis for two days. On March 27, she received 1.1 gm. of the powdered leaf; on March 28,

Fig. 5.—Case 2. Three usual leads; left bundle-branch block. Numerous curves of precisely similar form were obtained before and after the periods of tachycardia. Duration of ventricular complexes is indicated in Lead I.

0.4 gm.; on the morning of March 29, 0.2 gm. Several hours after this last dose, the heart rate was found to be much more rapid; an electrocardiogram was taken and revealed the alternating type of mechanism reproduced in Fig. 6. Paroxysms of tachycardia of this type occurred with decreasing frequency for three days, and then ceased. Electrocardiograms showed a return of sinus rhythm, with left bundle-branch block (Fig. 5). Digitalis was resumed on April 1; 0.2 gm. was given on April 1 and 2, 0.4 gm. on the fourth, and 0.2 gm. on the fifth. On the morning of the seventh, paroxysmal tachycardia was again present, and it occurred frequently for three days. Electrocardiograms showed the same type of alternating mechanism as that observed during the earlier days of the disorder. By April 11 the usual cardiac mechanism had been resumed, and neither paroxysms of tachycardia nor ectopic beats were detected during the remainder of her life. She died two weeks later, apparently as the result of pulmonary infection subsequent to infarction of the lung.

Autopsy.—There was very slight edema of the ankles. The right pleural cavity contained a small amount of free fluid. The heart was much enlarged, weighing 695 gm. after injection of the coronary arterial system with barium gelatine. The left ventricular cavity was large and its wall greatly hypertrophied, measuring 18 mm. in thickness. In the ventricle were numerous small ball thrombi, attached to the wall by thin pedicles. All valves appeared normal. The myocardium showed no fibrosis on macroscopic examination, and the coronary arteries were patent.

Microscopic examination of sections from the ventricles revealed great hypertrophy of the muscle fibers. Striations were quite distinct. There was slight dif-

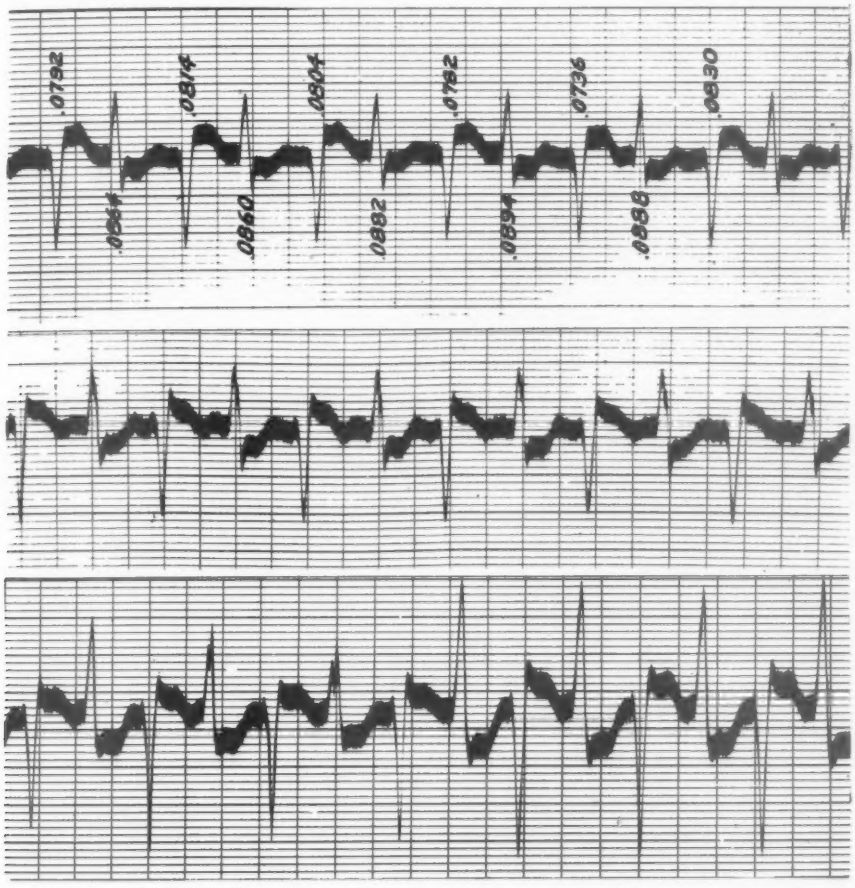

Fig. 6.—Case 2. Three usual leads, taken on April 8. Auricular waves not identified with certainty; ventricular rate varies from 163 to 180 per minute. Notice that the total duration of the ventricular deflections is less than in the preceding figure.

fuse increase in fibrous tissue. The small branches of the coronary arteries appeared normal, but in some of the larger branches there were sclerotic plaques and small accumulations of lymphocytic cells in and about the vessel wall.

Unfortunately, the examination of the conduction system could not be made as complete as desired, because the blocks of tissue removed for study did not include the bifurcation of the A-V bundle into its two main stems. Serial sections of a large portion of the interventricular septum were prepared; branches of the right and left divisions of the A-V bundle were identified readily, and presented

an extraordinary contrast in appearance. The tissue composing the right bundle-branch and its ramifications appeared entirely normal. The cytoplasm of the cells forming the left branch of the conduction system was vacuolated, extremely granular, and stained poorly. The cells appeared swollen; many contained no nuclei, while others contained only shadows of nuclei or pyknotic nuclear fragments. There was no cellular reaction of any sort surrounding the bundle-branch and its ramifications or infiltrating the adjacent myocardium. The general appearance suggested that the change was a degenerative rather than an inflammatory one, but the mechanism causing the lesion was not revealed in any of the sections.

Electrocardiograms.—Electrocardiograms were obtained at frequent intervals from the day of this patient's admission to the hospital until her death one month later. With a single exception, they were of two types only; they revealed the widened notched complexes typical of left bundle-branch block, with normal A-V conduction, or they showed paroxysmal tachycardia of the alternating type. Typical specimens of the two mechanisms are reproduced in Figs. 5 and 6, and the total duration of the ventricular deflections is indicated in corresponding leads.* Fig. 6 was selected from a number of similar records because the change in the form of the ventricular complexes in Lead III is greater than in any other electrocardiogram obtained. The only curve not conforming to the two types just

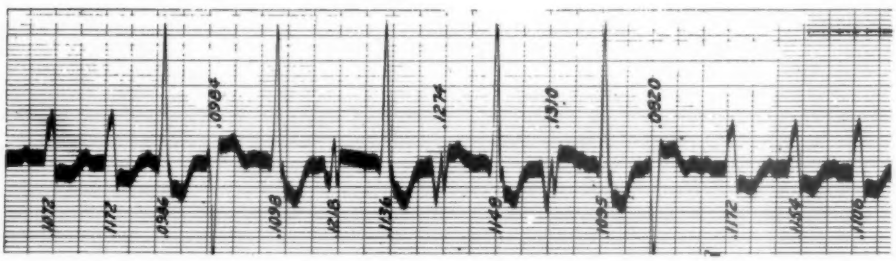

Fig. 7.—Case 2. Lead III, taken April 1. There are notable differences in the form and duration of the ventricular complexes during the short paroxysm. Auricular waves may be discerned in places through the paroxysm; their rate is 123.5 per minute, while that of the ventricles in 141.1. (x 2/3)

mentioned is shown in Fig. 7, which is from Lead III of a record taken April 1. It contains a complete short paroxysm of tachycardia in which the upward ventricular deflections are all alike, while the downward ones are of two distinct forms. The rate of auricles and ventricles during the preceding normal mechanism is 123.5 per minute; the auricular rate remains unaltered through the paroxysm, while that of the ventricles rises to 141.1 per minute. The typical bundle-branch block complexes are present immediately upon the conclusion of the paroxysm; there are no transitional forms.

Comment.—In considering the probable relationship between the administration of digitalis and alternating ventricular tachycardia, the case just presented is of peculiar importance, and seems to indicate fairly clearly that the relation was that of cause and effect. Tachycardia first appeared during the course of digitalis therapy, after 1.7 gm. had been given, and ceased gradually when the drug was discontinued; the abnormal rhythm reappeared when digitalis was again administered, and ceased when digitalis was stopped. The other

*All intervals marked upon the figures were measured by means of a comparator.

medication employed in this patient cannot reasonably be suspected of having caused the tachycardia; luminal and codeine sulphate were used freely during the first two days after her admission, novasurol was given once on April 4, three days after the first series of paroxysms occurred and three days before the second, and a single dose of theocin was given on the day of the first paroxysm. The last two drugs were administered later, in larger doses, without any effect upon the cardiac mechanism.

The electrocardiographic curves appear to be of the utmost significance in elucidating the nature of the mechanism responsible for the alternating tachycardia; this aspect of the matter will be fully discussed in the latter portion of the paper. So far as is known, this is the first recorded example of this type of tachycardia in a patient with preexisting bundle-branch block.

CASE 3.—A woman, forty-two years of age, entered the hospital on August 22 for the relief of symptoms of advanced congestive heart failure. Dyspnea and orthopnea had been noted about a year previously; edema of the lower extremities appeared shortly afterward. Symptoms became less following great restriction of physical activity. Four months before her admission, she contracted a severe respiratory tract infection, with fever, cough, and expectoration; shortly after the beginning of this infection, dyspnea and orthopnea reappeared and edema increased. All symptoms became gradually more severe from that time until she came to the hospital. The past history contained no facts of apparent significance.

The patient looked sick. There was orthopnea and slight cyanosis. Respirations were hurried and shallow, but not labored. There was no engorgement of the neck veins when she sat upright. The heart was moderately enlarged, the rhythm fundamentally regular, with occasional premature beats; the rate was 130 per minute. The heart sounds were clear and of normal intensity; a soft systolic murmur was audible over most of the precordium. The lungs showed persistent crackling râles over the lower lobes; the liver edge was felt 5 cm. below the costal margin in the right midclavicular line, and was tender. There was considerable edema of the subcutaneous tissues of the lower abdomen, the lower back, and the lower extremities. The radial arteries were slightly thickened; the retinal arteries showed moderate sclerosis. The blood pressure was 170 mm. Hg. systolic, 130 mm. diastolic. The urine constantly showed a very faint trace of albumin, with epithelial cells and leucocytes and occasional hyaline and granular casts. The excretion of phenolsulphonephthalein in two hours and ten minutes after the intramuscular injection of 1 c.c. was 40 per cent; the nonprotein nitrogen of the blood was 35 mg. per 100 c.c. Examinations of the blood revealed nothing abnormal. The blood Wassermann reaction was negative. The clinical diagnosis was arteriosclerosis with hypertension and heart disease; congestive heart failure.

Course and Treatment.—The patient was admitted late in the afternoon of August 22. Her weight was estimated at 135 pounds without edema. She stated that she had not received digitalis; it was subsequently learned that she had received the drug in small amounts for several weeks immediately prior to her admission. On August 23, attempts were made to secure electrocardiograms, but the wiring to the ward was defective and only Lead III could be obtained. (She was in a ward not then provided with elevator facilities, and it was regarded as unwise to move her down the stairs to the laboratory on a stretcher, as would have been necessary to secure proper records.) The one record that was obtained on

that day, however, showed normal A-V conduction and infrequent ventricular premature beats; so digitalis was started in doses of 0.2 gm. of the powdered leaf twice a day. She received this dose for the five days beginning with August 23 except for a single dose, which was reduced to 0.1 gm.; a total of 1.9 gm. in five days.

On August 26 it was noted that the heart rate was 160 per minute and apparently perfectly regular. The patient was vomiting but had no other symptoms

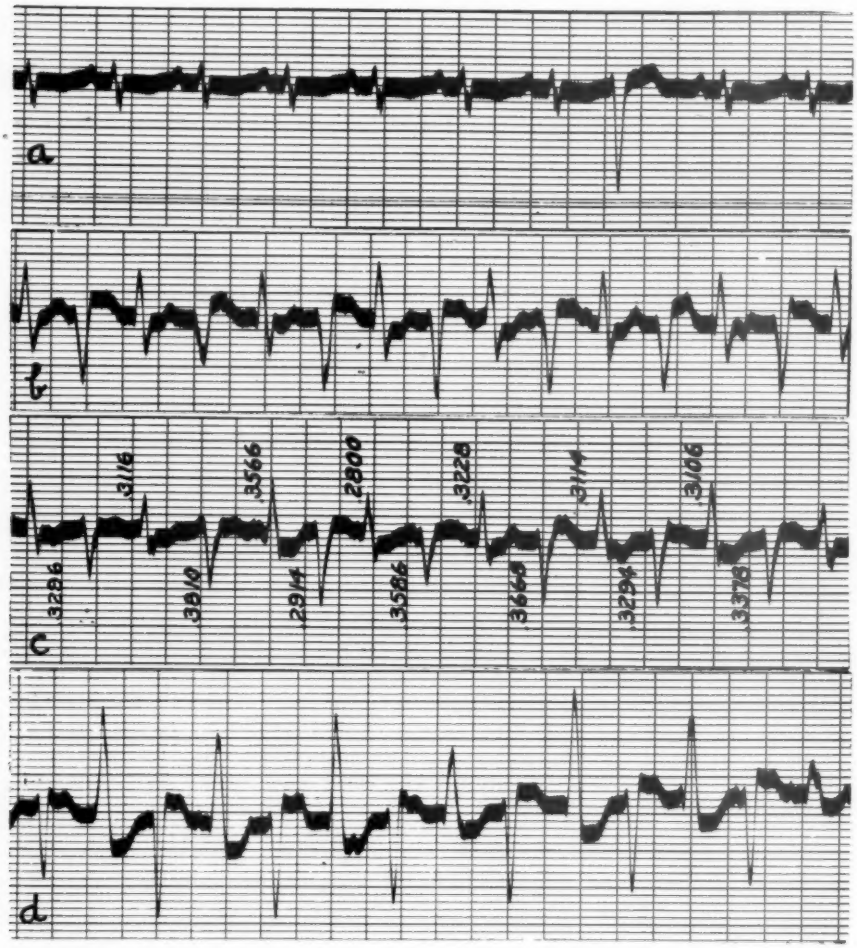

Fig. 8.—Case 3. The upper curve is of Lead III, taken Aug. 23; the lower three are the usual leads, taken Aug. 27. Auricular rate in the lower records is 200 per minute; ventricular rate varies from 171.4 to 184.6. The measurements in *c* are of the interventricular intervals. There are definite changes in form of occasional ventricular complexes, especially in Lead III.

of digitalis intoxication, and as she had been vomiting frequently for the two weeks before entrance to the hospital, as well as during the three days since entrance, this symptom was not regarded as significant. The rapid rate continued throughout the twenty-sixth and the twenty-seventh, so far as could be determined by frequent examination; it was not until the afternoon of the twenty-seventh that the electrocardiographic wiring was replaced and satisfactory records were secured.

Curves taken at that time revealed alternating ventricular tachycardia (Fig. 8); the probable rôle of digitalis was recognized, and the drug was permanently discontinued.

Vomiting continued to occur frequently, but it was apparently not due mainly to the digitalis, as it was present two weeks after all signs of digitalis effect upon the heart had disappeared. The original paroxysm of tachycardia ceased on August 28, but shorter paroxysms occurred with decreasing frequency during the two following days. None was observed thereafter until her discharge from the hospital on September 14, when she was in about the same condition as at the time of her admission. She died at her home two weeks later, apparently of congestive heart failure. Post-mortem examination was not performed.

Electrocardiograms.—In Fig. 8, *a* is shown a portion of Lead III, obtained on August 23, before the administration of digitalis was begun; it shows normal A-V conduction and a single premature beat arising in the ventricle. The three lower

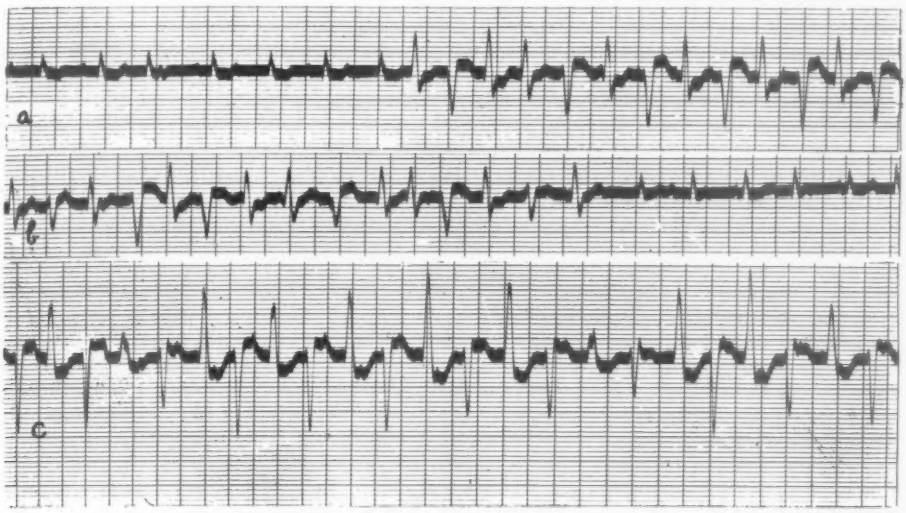

Fig. 9.—Case 3. *a* and *b* are from Lead I of two different curves taken on Aug. 28; they show the beginning and ending of a paroxysm. Partial A-V heart-block is present in the nontachycardial portions of these curves. *c* is from Lead III of the paroxysm that is shown beginning in *a*; note the occasional variations in size and shape of ventricular complexes. The auricular rate in Lead III is 203.2; the ventricular rate is from 190.8 to 193.4 per minute. (x 2/3)

curves are from one of the records of August 27 and portray the mechanism that apparently prevailed constantly for two and a half days—August 26, 27, and part of the twenty-eighth. Electrocardiograms were secured every few hours during the twenty-seventh and twenty-eighth, and the only differences in them were minor changes in the form of occasional ventricular deflections; changes that will be discussed presently. It is to be noted that there is both auricular and ventricular tachycardia, with complete dissociation of the two rhythms; the auricular rate is 200 per minute and that of the ventricles is from 171.4 to 184.6 per minute. Auricular waves can be clearly discerned in the central portion of Lead II and throughout most of Lead III.

On the evening of the twenty-eighth, the alternating ventricular complexes were not continuous; complexes of normal form were present in considerable numbers in response to auricular impulses, but with delayed A-V conduction. A selection

from a typical record of this period appears in Fig. 9, *a*, where the onset of a paroxysm is shown; partial A-V heart-block is present in the earlier portion of the curve. In the middle tracing of the figure, also Lead I, the offset of a paroxysm is registered, but from a record obtained some hours earlier than the upper curve. The lowest record of the figure represents the same paroxysm of which the beginning is shown in the upper record. The auricular rate during the paroxysms shown in

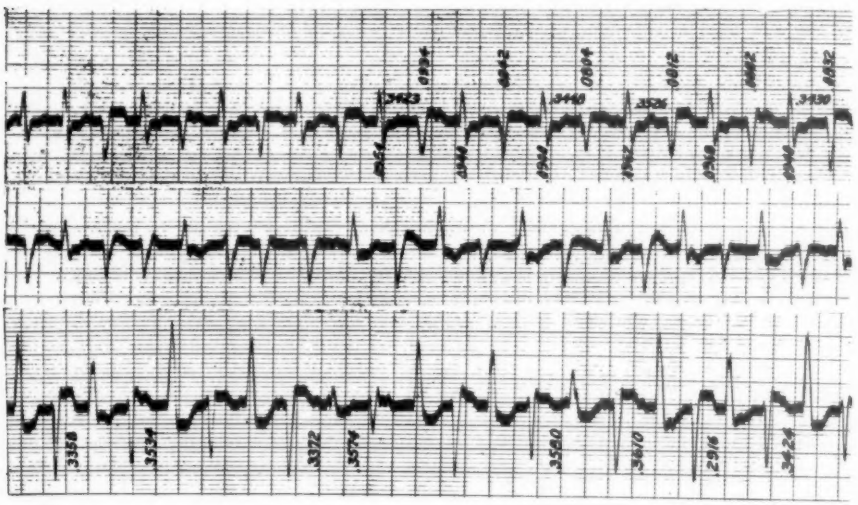

Fig. 10.—Case 3. Leads I, II, and III of one of the long paroxysms on Aug. 28. Measurements of the duration of ventricular complexes are shown in Lead I; the length of interventricular intervals is indicated in Leads I and III. It is to be noted that the degree of aberration of any complex bears no constant relation to the length of the pause preceding it. Auricular rate, 196.5 to 198; ventricular rate varies from 170.4 to 181.3 per minute. (x $\frac{2}{3}$)

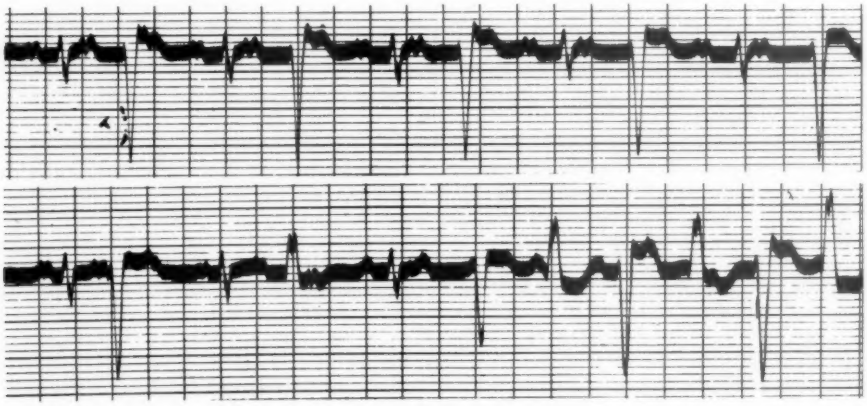

Fig. 11.—Case 3. Two portions of a single strip of Lead III taken on Aug. 29; the omitted intervening portion contained no ectopic beats. The upper curve shows regular coupling; the lower contains two ectopic beats and the beginning of a paroxysm of tachycardia composed of beats almost precisely like the preceding ectopic ones. The auricular rate is 200 per minute throughout; the ventricular rate during the paroxysm is 166.6 per minute.

this figure is from 196.5 to 200 per minute; the ventricular rate is from 183.3 to 192, the calculated rate depending upon the portion of the film chosen for measurement. The record displayed in *c* is inserted primarily to illustrate the differences in

the form of individual ventricular deflections that may occur without affecting the regularity of the alternation in direction.

Fig. 10 represents the three usual leads of an electrocardiogram obtained during one of the longer paroxysms. The change from an irregular to a regular alternation in the direction of the ventricular complexes is admirably shown in Lead II. Measurements of the actual duration of individual ventricular complexes are shown in Lead I; they are given for the sake of comparison with the measurements of the normal complexes in the same lead. The significance of the differences in the length of interventricular intervals, as indicated in Leads I and III, will receive comment in the later discussion. The auricular rate in this figure is from

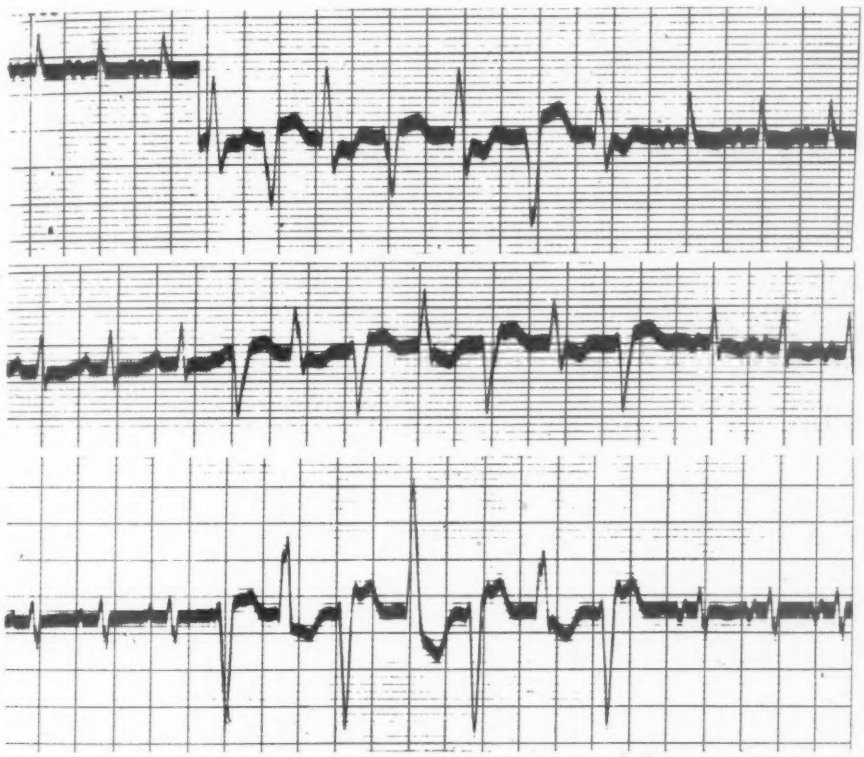

Fig. 12.—Case 3. Three usual leads. There is a brief alternating paroxysm in each lead. Note the change in the auricular waves after the paroxysm in Leads II and III. The initial beat of the paroxysm is clearly premature.

196.5 to 198 per minute; the ventricular rate is quite irregular and, in the measured portions, varies from 170.4 to 181.3 per minute.

Of considerable interest from the standpoint of the mechanism involved in the alternating tachycardia is Fig. 11. It represents two portions of a single strip of Lead III; five normal beats intervene between the two and are omitted to save space. In the upper curve there is perfect coupled rhythm, each normal complex being a response to each third rhythmic auricular impulse. The auricular rate is 200 per minute; the total ventricular rate is 128.5. In the lower half of the figure the second and fourth beats are ectopic, one of them identical with those shown in the upper curve and the other apparently arising in the opposite ventricle. The sixth complex of the lower curve ushers in a paroxysm of the alternating type,

and it is to be observed that the complexes which compose it are almost identical in form with the two ectopic beats preceding it. The auricular rate continues unchanged at 200 per minute throughout the paroxysm, while the rate of the ventricles at the onset of the tachycardia is 166.6.

Fig. 12 represents the three usual leads of an electrocardiogram obtained on August 30. A brief paroxysm consisting of seven beats is shown in each lead, and it is to be observed that the form of the auricular complex changes materially after the paroxysm in Leads II and III. The beat that initiates the paroxysm is in each instance clearly premature.

The final selection from the records of this patient is shown in Fig. 13. It represents the type of electrocardiograms obtained daily during the last two weeks of her stay in the hospital. In each lead ectopic ventricular beats are to be seen.

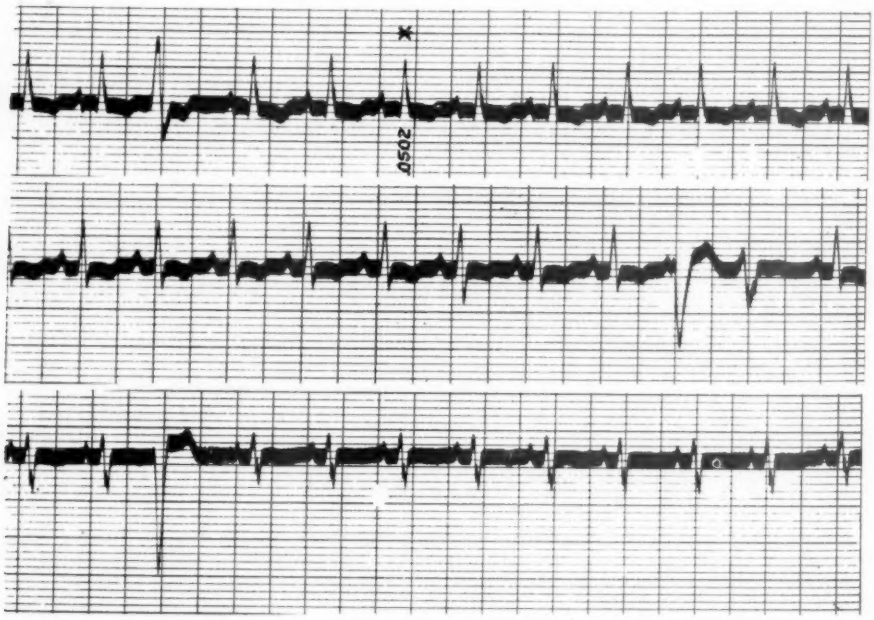

Fig. 13.—Case 3. Three usual leads, typical of the records obtained from Aug. 31 to Sept. 14. Normal mechanism with occasional ectopic ventricular beats. The complex in Lead I marked by an asterisk is the one measured for plotting as shown in Fig. 20. Note the striking similarity in form and size between the ectopic beats of this figure and those in corresponding leads during the paroxysms of tachycardia.

Comment.—The electrocardiograms obtained from this patient are of considerable interest. They may be described briefly as indicating a persistent tachycardia of both auricles and ventricles, with complete A-V dissociation, during the days when the action of digitalis was presumably at its height. During succeeding days the tachycardial periods became steadily less frequent and of shorter duration, and normal ventricular complexes began to make their appearance in response to auricular impulses, but there was partial A-V heart-block with dropped beats. (See Fig. 9, *a* and *b*.) This delay in conduction steadily became less, the responses to auricular impulses more numerous, until eventually normal mechanism was resumed, with oc-

casional ectopic ventricular beats. It is not proved, but seems extremely probable, that the events were related to the administration of digitalis and disappeared gradually as the drug was excreted from the body. The striking similarity between this case and that presented as Case 1 is worthy of emphasis; the same general comments might well serve for both.

CASE 4.—A woman, thirty-nine years of age, entered the hospital on November 23 because of shortness of breath and great swelling of the body and extremities. She stated that she was known to have had heart disease since the age of twelve or thirteen, but symptoms had appeared only two years previous to admission. For a year and a half there was dyspnea on exertion, but during the past six months edema had been present most of the time. She refused to restrict her activity until symptoms became so severe as to force her to remain in bed. During the past few weeks she had grown rapidly worse. The only fact of apparent significance in her past history was the occurrence of acute rheumatic fever in childhood.

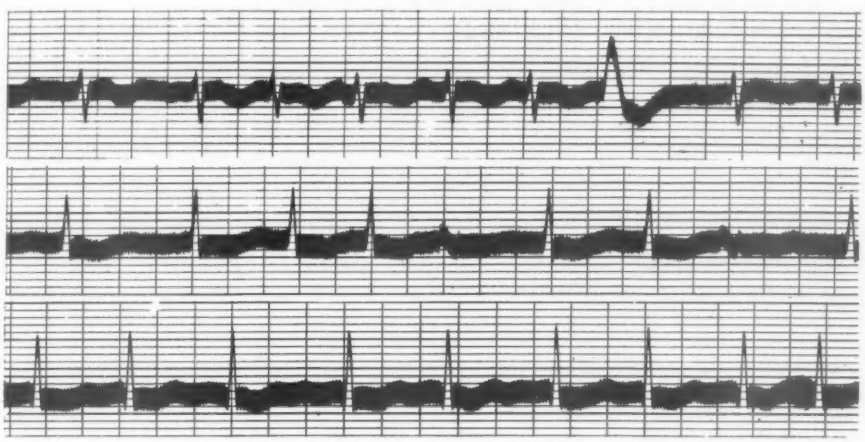

Fig. 14.—Case 4. Leads I, II, and III; auricular fibrillation, ectopic ventricular beats, right axis deviation, digitalis inversion of T-waves.

At the time of entrance to the hospital the patient was critically ill. There was extreme dyspnea, conspicuous cyanosis of lips and cheeks, and great engorgement of neck veins. The heart was considerably enlarged and presented the signs of stenosis and insufficiency of the aortic and mitral valves; the rhythm was totally irregular and the ventricular rate was approximately 150 per minute. There were signs of pulmonary and hepatic congestion, the abdomen was distended with fluid, and there was extreme edema of the lower trunk and lower extremities. The blood Wassermann reaction was negative.

Course and Treatment.—The patient was admitted at 1:40 A.M., Nov. 23. Her weight was 143 pounds. She received digifolin intravenously as follows: 5 c.c. at 2 A.M., 5 c.c. at 2:30 A.M., and 4 c.c. at 3 A.M., a total of 14 c.c., equivalent to 1.4 grams of the powdered leaf, within one hour. At 3:30 A.M., the heart rate had fallen to 78 per minute, and remained between 80 and 90 per minute until the afternoon of Nov. 24, when it was found to be between 90 and 100. She was therefore given 0.4 gm. of digitalis leaf by mouth at 8 P.M. On the following

morning the heart rate was found to be rapid and regular, and an electrocardiogram taken at this time showed paroxysmal ventricular tachycardia (Fig. 15) with a rate of 183.3 per minute.

From this time until her death three and a half days later there were frequent paroxysms of tachycardia, some of them lasting for several hours, most of them terminating abruptly after a few minutes. Between the paroxysms there was auricular fibrillation, with numerous ectopic ventricular beats. So far as could be determined by clinical observation, the patient was no worse during the long paroxysms than during the periods of auricular fibrillation with normal ventricular rate. Death occurred at 2:20 A.M., Nov. 29, two days after signs of pulmonary infarction had appeared over the right lower lobe.

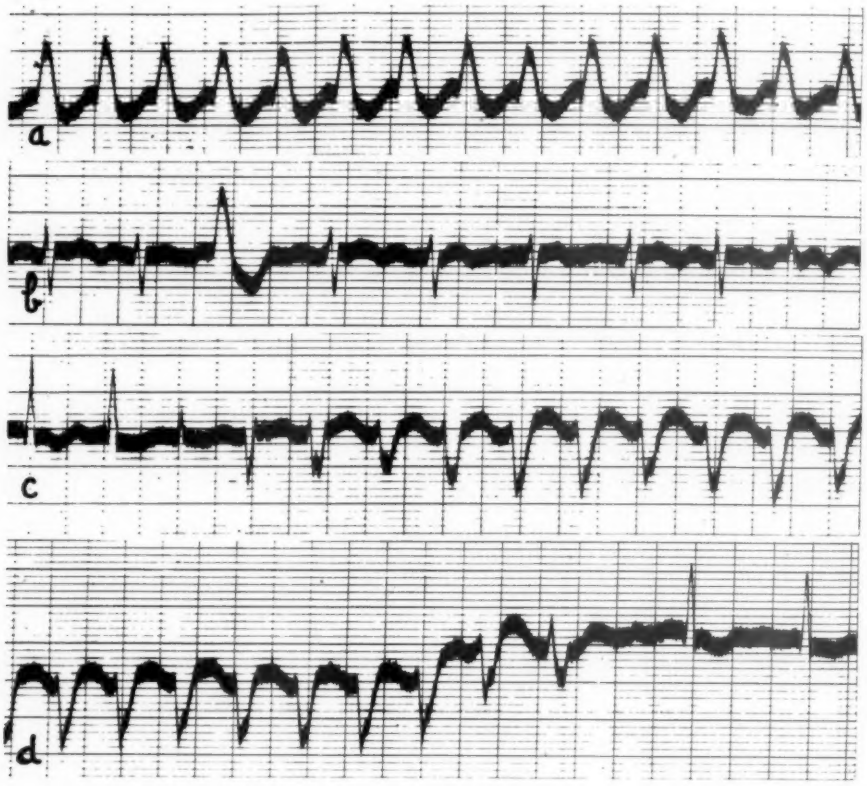

Fig. 15.—Case 4. *a* and *b*, Lead I during and just after the usual type of paroxysmal tachycardia. *c* and *d*, Lead III showing onset and offset of a similar paroxysm. The isolated ectopic beats in Lead I are closely similar to those which compose the paroxysm in the same lead.

Autopsy.—There was extreme edema of the entire body except the face. There was a large quantity of free fluid in the abdomen and in both pleural cavities. The parietal pericardium was firmly adherent to the left pleura, the diaphragm, and the sternum; the pericardial sac was obliterated by adhesions. The heart with its attached pericardium weighed 630 gm. The wall of the right ventricle was 6 mm. in thickness: that of the left was from 16 to 18 mm. There was a large mural thrombus in the right auricular appendage. The tricuspid and pulmonary valves were normal. In the left auricle there was a huge thrombus, 1 cm. in thickness, covering the entire wall except the small portion leading into the

funnel-shaped mitral orifice; the thrombus extended into and solidly filled the greatly dilated left auricular appendage. There was advanced stenosis of the mitral orifice, the opening measuring 1 cm. by 0.5 mm., lying at the bottom of the rigid funnel typical of extreme stenosis. The tissues surrounding the slit-like opening were rigid and calcareous. The papillary muscles were greatly hypertrophied; the chordae tendinae were shortened and very thick. The aortic orifice was triangular in shape and measured less than 4 mm. in its greatest diameter. The valve cusps were fused and greatly thickened. The intimal surface of the aorta appeared normal.

Over most of the right lower lobe of the lung the pleura presented the picture of acute inflammation. The lung tissue of that lobe showed extensive infarction. The branch of the pulmonary artery supplying that portion of the lung was almost closed by a thrombus which extended for several centimeters along the vessel and was firmly attached to the wall.

The microscopic sections of the heart revealed both acute and chronic inflammatory processes in the pericardium. The muscle fibers were extremely hypertrophied, with irregular gigantic nuclei. There were small scattered areas of fibrosis. There was diffuse infiltration of the interstitial tissue, especially in the left ventricle, with mononuclear and polynuclear cells. Typical Aschoff bodies were present.

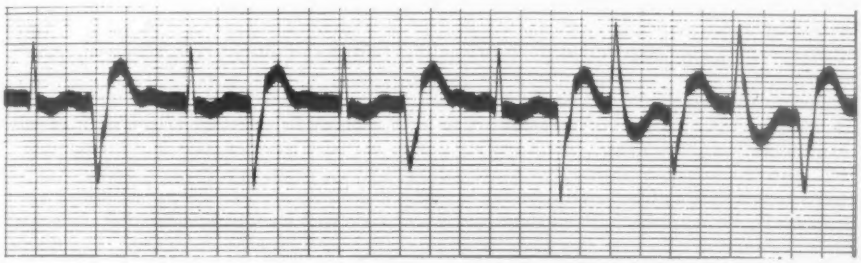

Fig. 16.—(x 9/11) Case 4. Lead III, showing a period of coupled rhythm followed by the onset of a paroxysm of tachycardia. The downward deflections of this paroxysm are almost identical in form and size with the preceding ectopic beats.

There was a widespread acute inflammatory process in and about the walls of the smaller coronary arteries, and a similar process in the wall of the left auricle; in this chamber, the inflammation extended to the endocardial surface, which was entirely covered by thrombus.

Comment.—In this case, as in the preceding one, we have to deal with paroxysms of tachycardia arising in ectopic foci and apparently bearing a definite relation to the administration of large doses of digitalis within a short time. Most of the recorded paroxysms in this case were of the form shown in Fig. 15; it is unfortunate that only a few beats of the alternating mechanism were successfully photographed, but there can be little question that the last few cycles of Fig. 16 represent the same type of abnormality as that shown in the preceding cases.

CASE 5.—A man, seventy-four years of age, entered the hospital on May 15 because of weakness, difficulty in breathing, and swelling of the body and extremities. Symptoms had first been noted about four years previously, and had grown gradually but steadily more severe until one year before his admission,

when he had to abandon work. For the past nine months he had been forced to sit upright in order to breathe. During the several weeks immediately preceding his entry, he had become very much worse.

Examination showed extreme cyanosis of face, hands, feet, and mucous surfaces. There was orthopnea and dyspnea, and a frequent productive cough. The heart was greatly enlarged, the apex impulse being in the anterior axilla in the sixth intercostal space, and the right border of percussion dullness 4 cm. to the right of the median line in the fourth intercostal space. The rhythm was regular, the rate 100 per minute. There was a soft systolic murmur in the region of the apex. There was advanced sclerosis and tortuosity of the peripheral vessels; the blood pressure was 190 mm. Hg. systolic, 110 mm. diastolic. There were signs of congestion at the bases of the lungs, the liver edge was 8 cm. below the costal border in the right midclavicular line, and there was evident ascites. The entire body below the level of the lower ribs was extremely edematous. The blood Wassermann

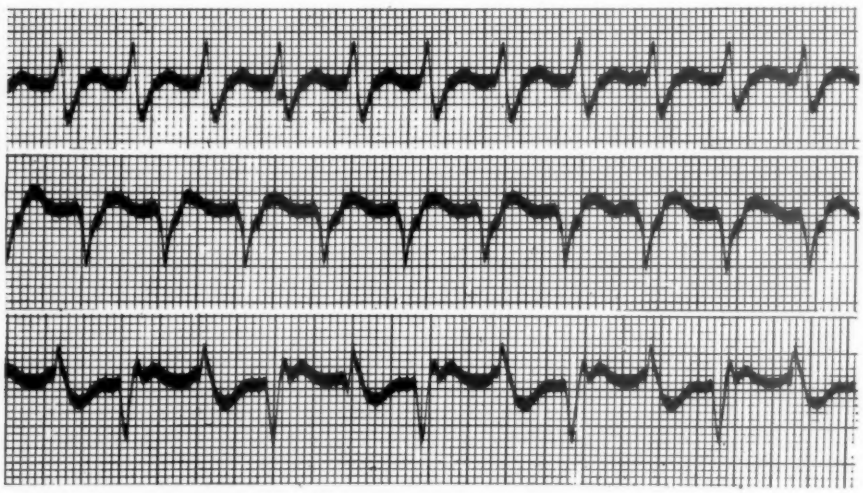

Fig. 17.—Case 5. Three usual leads. Alternation in the direction of the ventricular deflections occurs in Lead III only. Auricular waves cannot be discerned. The ventricular rate is 150 per minute in Lead I, 144.4 in Lead II, and 156.52 in Lead III. No records were obtained from this subject after the conclusion of the tachycardia.

was negative. The clinical diagnosis was arteriosclerosis and hypertension with heart disease; advanced congestive heart failure.

Course and Treatment.—The patient was admitted late in the afternoon of May 15. His weight was not determined; it was estimated at about 160 pounds with edema. He received the tincture of digitalis by mouth as follows: May 15, 9 c.c. at 8 P.M., and 4 c.c. at midnight; May 16, 4 c.c. at 4 A.M., at 8 A.M., and at noon: a total of 25 c.c., equivalent to 2.5 gm. of the powdered leaf, within a period of sixteen hours. Late in the afternoon of May 16, the heart rate was noted as very much more rapid than it had been in the morning; the tachycardia was still present on the following day, and an electrocardiogram was obtained (May 17). It showed, in Lead III only, the alternating type of tachycardia with which this paper is concerned. Leads I and II of that figure are regarded as probably indicating paroxysmal ventricular tachycardia, although they might equally well represent paroxysmal tachycardia of junctional origin; the widening and notching of the ventricular complexes in that event would be regarded as indicating pre-existing bundle-branch block or as due to aberration induced by the

rapid rate. Unfortunately, no record was obtained before or after the tachycardia, so no decision as to the nature of the mechanism is possible. The rapid rate continued apparently without change, until the evening of May 17, and was again present for several hours on the day following.

The patient grew steadily worse and died on May 20. Permission for post-mortem examination was not granted.

Comment.—The study of this patient was far from complete, but it has seemed desirable to include his record with the others because it serves to emphasize the same time-relationship between the administration of digitalis and the onset of paroxysmal tachycardia of a very unusual type. An elderly man, he received an amount of digitalis greatly in excess of the calculated requirement, and received it within an extremely short time. A few hours later the heart was being driven by a new mechanism which persisted for the better part of two days. It is not known whether this new mechanism was of the alternating type most of the time, or whether alternation occurred only infrequently; nor is it a matter of great consequence. The important fact is that in this patient, as in the four preceding ones and in all similar recorded cases, the alternating type of ventricular deflections occurred during paroxysms that were apparently induced by large doses of digitalis. The complete evidence will be considered in a moment.

DISCUSSION

As stated earlier, the chief reason for placing the accompanying curves on record is that they appear to yield information as to the nature of the tachycardia. We are now in position to consider briefly the important features of the electrocardiograms and to summarize the evidence they provide as to the location of the pacemaker during the periods of tachycardia with regular alternation of upward and downward ventricular deflections. It is to be reemphasized that we are not now concerned with other forms of ventricular tachycardia, such as that shown in Fig. 15, nor with other disturbances of rhythm that may prevail occasionally in the same patients, except in so far as they serve to throw additional light upon the main point. The curves reproduced have been selected from the large number available in an effort to illustrate the origin of the new mechanism rather than the numerous minor differences that may occur from day to day in the form of the ventricular deflections during such paroxysms. It is recognized that Case 5 has no importance in this respect. The following discussion is based, therefore, largely on the first three cases presented; the last two have been included because they strengthen the evidence in respect of the rôle of digitalis. The evidence will be discussed as a whole instead of separately for each patient.

It seems clear that the impulses responsible for the rapid ventricular rate may conceivably arise either within or above the ventricles.

If within the ventricles, they are presumably generated alternately in right and left chambers; if above the ventricles, they are presumably transmitted alternately over right and left divisions of the bundle, with partial or complete blocking of transmission over the other branch. These two possibilities have been recognized by all who have discussed the matter[5, 6, 7]; there is a third one which will be considered later.

Now the form of the ventricular complexes during these paroxysms is very similar to, and in many instances identical with, that of ectopic beats arising in the ventricles, rather than with the complexes seen in instances of known bundle-branch block. The total duration of the ventricular deflections is frequently within normal limits, and there may be complete absence of the characteristic notching observed in the clinical curves of bundle-branch lesions, and regarded as indicating spread of the impulse to the homolateral ventricle. This fact has been mentioned by Felberbaum as an argument against a supraventricular origin of impulses. But the argument rests upon the assumption that there is *complete* blocking of impulse transmission alternately on right and left sides, and it is far from certain that such an assumption is justifiable. It may be assumed, with equal reason, that there is a delay in bundle-branch conduction, without complete blocking, due to lengthening of the refractory period of the branches, with consequent alternating preponderance of right and left ventricular effects. This possibility has been emphasized in connection with the examples of changing ventricular complexes in complete heart-block reported by a number of observers and thoughtfully discussed by Korns[8] and by Gilchrist and Cohn.[9] Korns concludes that the change from upward to downward ventricular complexes in his case of auricular fibrillation with high grade A-V heart-block is due to variations in the refractory period of the bundle-branches, a constant focus of impulse formation being above the bifurcation of the bundle; Gilchrist and Cohn regard the changes in the direction and form of ventricular complexes in their patients as due to a shifting of the impulse center from one side of the bundle division to the other. The experimental work of Wilson and Herrmann[10] strongly suggests that the latter explanation is the more likely one in cases where the changes in the ventricular complexes are associated with complete heart-block. A detailed consideration of the two views would carry us far afield and is not necessary at present, for the curves here presented afford definite evidence in favor of one of them. It is important to point out, however, that the evidence derived from the mere form of the complexes is not decisive.

An indication that the new pacemaker probably resides within the ventricles is found in the irregularity of rate during the maintenance of the paroxysm. Luten has argued, and logically, that the absolute

regularity of rate in his curves is in favor of a single focus of impulse formation, rather than separate foci in the two ventricles. The argument loses force if it can be shown that regularity is not an invariable, nor even a frequent, characteristic of the paroxysms. Paroxysms of tachycardia arising in the supraventricular tissues are notable for their regularity[11]; those arising in the ventricles are often slightly but distinctly irregular, as has been pointed out by several authors[3, 12] and emphasized by Strong and Levine.[13] Irregularity is a feature of practically all paroxysms registered in the patients here reported; in some of the accompanying curves the variation in interventricular intervals is sufficiently great to be apparent on casual inspection; in others, careful measurements disclose significant differences. (See Figs. 1, 8 *c*, and 10.) This irregularity is regarded as an indication that the ectopic impulses arose within, rather than above, the ventricles.

In the second place, curves obtained from several patients between paroxysms exhibit typical and unquestionable ectopic beats arising in one ventricle, and these beats are similar in form and size to those of the paroxysm which are in the same direction. The occurrence of beats which can be unhesitatingly identified as originating in the ventricle, and their close similarity to beats later occurring in rapid sequence, speaks strongly for a common site of origin of the two. This point has been emphasized by Robinson and Herrmann[1] as important in distinguishing between paroxysmal tachycardia arising in the ventricles and that arising in the supraventricular tissues; it has also been stressed by Felberbaum, whose patient showed isolated ectopic ventricular beats. Occasionally it is possible to compare, in the same lead, isolated ectopic beats and those which initiate a paroxysm of tachycardia; in most such instances (Figs. 3 *c* and 16) it is found that these single ectopic beats stand in the same relation to the preceding normal beats as do the initial beats of the paroxysm to the normal beats that precede them.

There is considerable variation, even in a short stretch of the paroxysm, in the form of the ventricular complexes, variations which might be thought to represent varying time-relations of the levo- and dextrocardiogram. These variations are usually not sufficiently great to permit the statement that they afford evidence of intraventricular origin of impulses, for similar alterations may conceivably occur when the ventricles are responding to supraventricular impulses if there are variations in the refractory period of the bundle-branches (Korns). In some of the curves, however, there are occasional beats which, while preserving their regularity of alteration, show such conspicuous alterations in form as to make it improbable that they arose in the same focus as those which stand on either side of them. (See especially Figs. 8 *d*, 9 *c*, and Lead III of Fig. 10.) If it is assumed that these

complexes all represent responses to supraventricular impulses, with alternate refractoriness of right and left bundle-branches, then the change in form of any beat should bear a fairly constant relation to the length of the time interval preceding it—in other words, the shorter the diastolic pause, the greater should be the change in the complex that terminates it. But this is not the case; some of the most extreme alterations occur after pauses as long as, or longer than, those which precede the unaltered complexes. This is true whether the time interval between successive complexes is considered, or only the interval between successive complexes in the same direction. This variation in form may be satisfactorily explained on the assumption that the beats arise alternately in the ventricles, but not always at precisely the same level of the conduction system; it is very difficult to explain it upon the assumption that they arise above the bifurcation of the bundle.

The second case provides additional evidence bearing upon the origin of the impulses during the paroxysms of tachycardia. This patient was known to yield curves characteristic of left bundle-branch block; numerous examples were obtained before and after the occurrence of the tachycardia, and all were alike. Now if it is assumed that the pacemaker during the tachycardia is above the bifurcation of the A-V bundle, it is necessary to assume further that impulses reach and involve the conduction system of one ventricle before that of the other, and that they do so in an alternating fashion. Expressed otherwise, the assumption is that the first impulse reaches the left ventricle before it does the right, the second reaches the right ventricle before it does the left, and that the stimulation continues in this manner. This is a vital and inevitable part of any explanation that assumes the location of the pacemaker above the bifurcation of the bundle, for the initial portions of alternate complexes in these curves represent right and left ventricular effects. But in this patient it is impossible for any impulse originating above the ventricles to reach the left ventricle before it does the right, because, in the presence of left bundle-branch block, such impulses can reach the left ventricle only by spreading through the interventricular septum from the conduction system of the right ventricle. The only conceivable manner in which the left ventricle can be involved *first* is for the impulse to originate in that chamber below the level at which the bundle-branch is injured. That this is the probable event is also indicated by this consideration: the average duration of the ventricular complex of this patient when the heart is responding to sinus impulses is approximately 0.11 second (Fig. 5). This figure may safely be taken as indicating the least possible time in which an impulse can pass through the conduction pathway of the right ventricle and spread through the septum to involve that of the left; if

the time is altered by rapid beating it will be increased rather than shortened; a known and frequent effect of simple paroxysmal tachycardia is to widen the ventricular complexes. Yet it is found that the ventricular deflections during the paroxysms of tachycardia in this patient are of much shorter duration than those during the normal sinus rhythm; by actual measurement they average approximately 0.08 second, or about 0.03 second less than the nonparoxysmal beats in the corresponding lead (Fig. 6). This is a conspicuous and significant decrease; it can be explained in but one way, namely, that impulses are arising within the ventricles.

The occurrence of auricular waves during paroxysms of tachycardia, distinct from and at a slower rate than the ventricular complexes, has been mentioned not infrequently since the appearance of Robinson and Herrmann's paper[1] as an indication that the paroxysms in question are of ventricular origin. It may certainly be regarded as an indication that the paroxysm did not arise in the auricle, but it is by no means clear that the presence of auricular waves excludes the possibility of origin in the junctional tissues. For this reason, and because the question of auricular origin has not arisen in connection with any case of alternating ventricular tachycardia, no emphasis has been laid upon the occurrence of rhythmic auricular summits in the present curves.

There is a final test which may be applied in an effort to determine whether the ventricular complexes in these electrocardiograms represent beats arising in the ventricles, or aberrant responses to supraventricular impulses. Lewis[14] has shown that the normal ventricular complex is a summation of right and left ventricular effects; that if these effects are separated by producing first a temporary block of the right bundle-branch and then of the left, the algebraic summation of the corresponding electrocardiographic curves will yield complexes identical in all important respects with the normal ones. In order to apply this test it is necessary to plot out the complexes accurately to scale. This has been done for the curves of Cases 3 and 2; the method is sufficiently indicated by Figs. 18, 19, and 20. The third and fourth ventricular deflections from the right-hand end of Lead I in Fig. 8 have been carefully and repeatedly measured by means of a comparator, and plotted to scale as shown in Fig. 18, *A* and *B*. The complex resulting from their algebraic summation in their presumably normal time relations is shown in Fig. 19, and is to be compared with the outline of the known normal for that lead, shown in Fig. 20. The measured normal complex is the third one following the ectopic beat in Lead I of Fig. 13; it is marked by an asterisk. The wide divergence of the two outlines needs no comment.

But it is not sufficient thus to summate the plotted figures in their apparently normal time relations; they must be shifted with refer-

ence to each other to ascertain if any possible combination of the two will result in a complex of normal outline, for if there is merely a delay in conduction along the bundle-branches, instead of complete block, the complexes will represent advancement or retardation of the levo- or the dextro-cardiogram. The procedure is made clear by the figures given in the paper of Gilchrist and Cohn.[9] These further steps have been carried out in detail but have not been illustrated. It will suffice to say that the plotted outlines have been

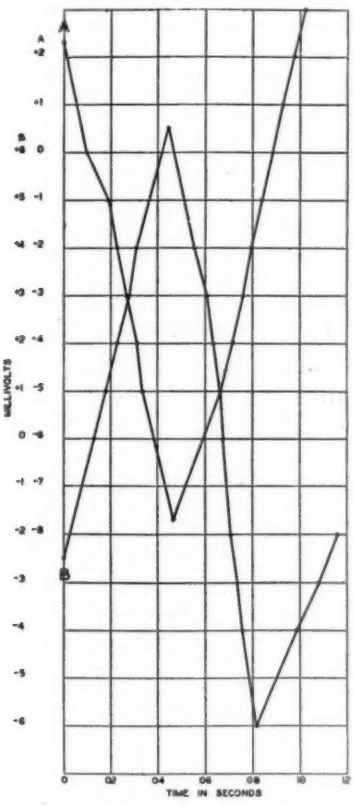

Fig. 18.—Typical upward and downward ventricular complexes of the paroxysms of Case 3 have been redrawn to scale. *A* represents the fourth complex from the right hand end of Lead I in Fig. 8; *B* represents the one immediately following.

moved with reference to each other so that first the levo-cardiogram and then the dextro-cardiogram took precedence, the shift being 0.02 second at a time, until the divergence from the normal became steadily greater. It was found impossible to arrange them in such a relation that their summation resulted in an outline resembling the normal.

The same procedure has been followed with the deflections of Figs. 5 and 6, although it seemed clear for the reasons already given that these ventricular complexes could not represent responses to supra-

ventricular impulses. It was again found impossible to place the plotted outlines in any relation such that their summation would yield the widened complex representing the invariable response to supraventricular impulses in this patient.

The complexes in Fig. 1 have not been similarly plotted because it is clear at a glance that the actual value of the downward deflections in Lead I is much greater than that of the upward deflections; it is impossible that their algebraic summation should result in a purely

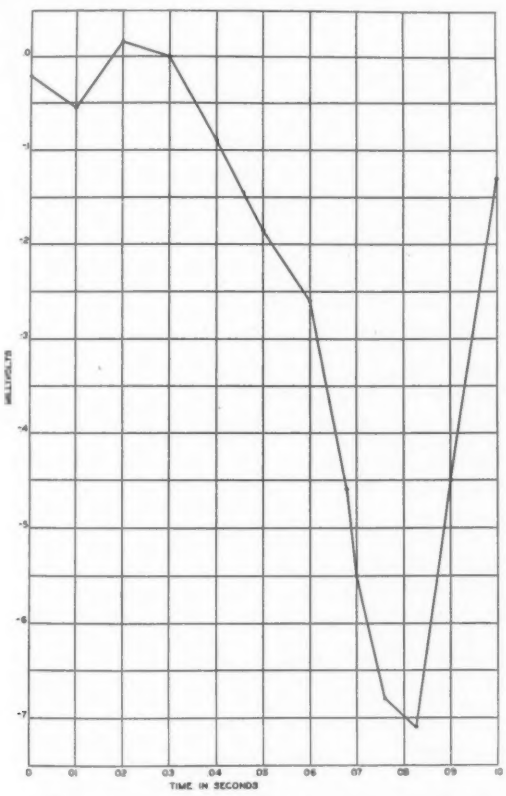

Fig. 19.—The curve which results from the algebraic summation of the outlines in Fig. 18 in their presumably normal time relationship. This is to be compared with the known normal complex for this lead, shown in Fig. 20.

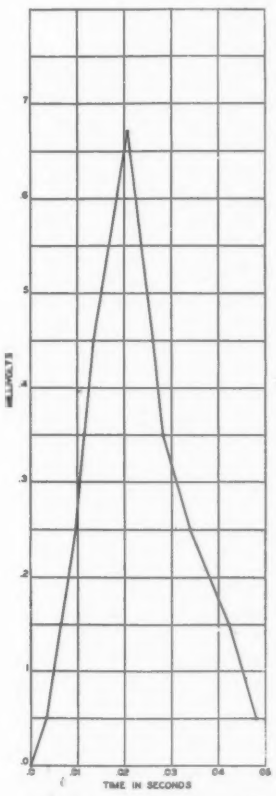

Fig. 20.—A normal complex of Lead I of Case 3 redrawn to scale. The actual complex chosen is that indicated by an asterisk in Fig. 13.

upward complex, no matter how the two outlines might be placed with reference to each other. Yet the known normal complex for this lead is an upward one (Fig. 4). Precisely similar arguments apply to Lead III of Fig. 1, in which the net value of the upward complex is nearly three times that of the downward one. The two measurements cannot possibly combine in such a way as to produce a downward complex; yet the known normal for this lead is downward.

For the reasons just given, it is regarded as fairly certain that the ventricular deflections in these three patients do not represent either partial or complete blocking of supraventricular impulses in the bundle-branches, that is, they are not actually levo- and dextro-cardiograms, nor even a summation of the two in differing time-relations. This is important evidence that the impulses responsible for these deflections actually arise within the ventricles.

Nature of the Paroxysmal Tachycardia.—If the evidence just presented is accepted as indicating that the abnormal mechanism has its origin within, rather than above, the ventricles, there is a further possibility that requires consideration, although, being largely hypothetical, it need not receive extended discussion. It is that the mechanism responsible for this curious disorder is a circus movement in the ventricle; that there is a circulating wave of excitation, similar to that occurring in the auricle in cases of auricular flutter and auricular fibrillation, pursuing a path relatively fixed and constant through the ventricular tissue, but not necessarily in the same plane in different patients or in the same patient during different paroxysms. The possibility is suggested by several characteristics of the curves, but it is supported mainly by the following considerations. Levy and Lewis[15] have obtained, from experimental animals under chloroform anesthesia, curves precisely analogous to those illustrating the present paper and have stated that this type of rhythm preceded the onset of ventricular fibrillation by only a few seconds. In a later paper, Levy[16] again explicitly states that the tachycardia characterized by alternate upward and downward ventricular complexes (regarded by him as extrasystoles generated alternately in right and left ventricles) often terminates in ventricular fibrillation, and the actual transition from one to the other is clearly depicted in his Fig. 4. Furthermore, Reid[4] has published records from a human case illustrating alternating tachycardia followed within a few seconds by ventricular fibrillation; the actual transition was not photographed. The number of instances in which this alternating tachycardia has been recorded in either human beings or experimental animals is small, yet it seems clear from these examples that there is a close relationship between the tachycardia and ventricular fibrillation, and it is at least conceivable that they represent earlier and later stages of the same disorder. Now there are many reasons for believing that ventricular fibrillation is due to circus movement in the ventricle; the evidence in support of that belief is so strong that it has led to general acceptance; it is lucidly and convincingly summarized by Lewis,[17] and need not be repeated here. If alternating tachycardia is closely related to ventricular fibrillation, and fibrillation is due to circus movement, it is possible—even probable—that the tachycardia is itself due to the same mechanism. The comparative regularity of the complexes and their relative constancy of

form during the alternating tachycardia would make it necessary to regard it as more nearly analogous to auricular flutter than to auricular fibrillation; that is, the circulating excitation wave pursues a longer and more nearly fixed path in ventricular tachycardia than in ventricular fibrillation. There is apparently nothing in the accompanying curves or in the known facts regarding ventricular fibrillation inconsistent with the belief that both may be due to the same fundamental mechanism.

The suggestion has been made briefly by others[2] that paroxysmal ventricular tachycardia of the usual form (in which there is no alternation in the direction of the ventricular complexes) might be due to circus movement. The facts supporting such a belief have been marshalled and carefully considered by Lewis,[18] who concludes that the evidence is not sufficiently decisive to warrant a final statement. It is believed that the relationship between the *alternating* tachycardia and circus movement is a little closer than that between the usual paroxysmal tachycardia and circus movement, because in the former case the actual transition to ventricular fibrillation has been shown to occur.

The argument need not be pressed, for it has not yet been finally proved that ventricular fibrillation is in fact due to circus movement, although the evidence is so overwhelming as to admit of little doubt.

Rôle of Digitalis.—The part played by digitalis in the development of this abnormal rhythm may be indicated briefly. It is known that digitalis often causes ectopic ventricular beats as an early manifestation of intoxication; it is known that ectopic beats in such circumstances may be increased in frequency up to the point of regular coupled rhythm by continued administration of the drug; it is known that ventricular fibrillation may be provoked in experimental animals by its intravenous injection.[19] There is strong evidence that excessive doses often cause paroxysms of ventricular tachycardia of the type usually encountered, in which the complexes are of one form.[4] When these suggestive facts are coupled with the observation that in every instance here reported and in all those previously observed, the disturbance followed the administration of large amounts of digitalis, and that in one patient tachycardia disappeared when the drug was stopped, only to reappear when it was again given, there can be little question that this form of tachycardia owes its inception to the administration of excessive quantities of the drug.

The relation of the dose of digitalis to the body weight cannot be ascertained precisely in any of the five patients. If the theoretical amount required for therapeutic effects is calculated on the basis of body weights, according to the well-known method of Eggleston, it seems clear that excessive quantities were given to the patients presented as Cases 1 and 5. But these patients were weighed while

edematous; the actual body weight was estimated, and was thought to be not more than 115 and 140 pounds, respectively. The second and third cases had received digitalis before admission to the hospital, the exact amounts being unknown; the total dose, therefore, cannot be definitely stated. The weight of the fourth patient was probably 120 pounds or less, and she received 1.4 gm. of digitalis within a period of one hour, without apparent ill effects. A single dose of 0.4 gm. forty-one hours later was followed by paroxysms of ventricular tachycardia. Even if it is assumed that the total amount (1.8 gm.) was present and active in the body at one time, the dosage is not greatly in excess of the calculated requirement. It must be kept in mind that amounts as large as, and even larger than, those used in the present cases have been administered to other patients without the subsequent development of alternating ventricular tachycardia. Careful consideration of the doses and the circumstances in which they were used leaves the impression that there are probably factors other than the total amount of digitalis which may be responsible for the onset of the mechanism under discussion.

It is possibly of significance that all of the patients mentioned in the present paper suffered from advanced congestive heart failure; it may be questioned whether similar doses of digitalis would have precipitated tachycardia in hearts less severely injured. Whether the size of the heart is an important factor is not clear; it is possible that only enlarged hearts are capable of spontaneously originating and sustaining a mechanism thought to depend upon circus movement in the ventricle; that is suggested by the observations of MacWilliams[20] and of Garrey,[21] and by the fact that all recorded examples of the alternating tachycardia occurred in patients with very considerable enlargement of the heart.

It is of some interest that three of the five patients did not suffer from headache, nausea, or vomiting. The record of one of them does not mention these symptoms and presumably they were absent, but a definite statement is not warranted. These symptoms occur with such uniformity as early manifestations of intoxication, that there is an apparent tendency to believe that digitalis may safely be given until they appear. Such a rule may possibly be followed with safety if the drug is given relatively slowly over a prolonged period; that it may be unwise when large doses are used is sufficiently shown by the present cases. Yellow vision, mentioned as an occasional toxic manifestation of digitalis, did not occur in any of the first four cases here reported; it is not known whether it was present in the fifth.

From the standpoint of immediate practical application, the implications are clear. Any significant increase in heart rate, without an obvious physiological cause, in a patient who is receiving digitalis, or

any apparent failure of digitalis to slow the fibrillating heart, should be regarded with suspicion. In either case, digitalis should not be continued until an electrocardiogram has been secured.

SUMMARY

Five cases are reported in which there occurred paroxysms of tachycardia of a most unusual kind. These paroxysms consisted of regularly alternating upward and downward ventricular complexes. Only five similar examples have been recorded previously.

Reasons are given for believing that the paroxysms are due to ectopic beats arising alternately within the right and left ventricles; the possibility that circus movement in the ventricles may be responsible for this abnormal mechanism is briefly discussed.

In all of the recorded cases, this curious ventricular tachycardia seems to have occurred as a result of excessive doses of digitalis, although the usual symptoms of intoxication may be entirely absent.

The author wishes to express his thanks to Dr. Alfred E. Cohn, who kindly read the manuscript and made many suggestions for its improvement, and to Miss Mabel Carmichael for the preparation of the electrocardiographic prints.*

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*Since this paper was written, Palmer and White (Am. Heart Jour., 1928, iii, 454) have reported two other cases of this type of ventricular tachycardia, and have mentioned the three cases of Gallavardin (Arch. d. mal. du Coeur, 1926, xix, 153) unfortunately overlooked by the writer in reviewing the previous literature. Apparently Gallavardin was the first to suggest the possibility of circus movement in the ventricle as an explanation of this unusual type of tachycardia; Palmer and White have brought forward evidence in support of that view. The present paper has been allowed to stand as originally written because the evidence here presented is quite different from that of Palmer and White, although leading to much the same conclusions.

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COMPRESSION AND DISPLACEMENT OF THE BRONCHI IN MITRAL STENOSIS*

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INTRODUCTION

Enlargement of the left auricle is a very common event in mitral stenosis. It may reach considerable proportions and as a result various complications from distortion of the upper mediastinal contents may occur; for example, paralysis of the left recurrent laryngeal nerve, compression and displacement of the esophagus, changes in the outline of the right border of the heart and stenosis of the left bronchus, and spreading of the angle of the departure of the bronchi from the trachea. In this paper I wish to discuss the last condition.

Recently a patient came under observation in whom the results of narrowing of the left bronchus, due to compression by an enlarged left auricle, could be demonstrated. Since this is a rather unusual complication of mitral stenosis the case is being reported in detail.

REPORT OF CASE

F. C., a white man, aged forty-seven years, was admitted to the Medical Service of the University of Chicago Clinics January 5, 1928, complaining of "shortness of breath and pain in the left side." The family history was unimportant. He had enjoyed excellent health until a decade ago when he suffered from an acute febrile illness which was diagnosed as influenza during the great pandemic. He had never had rheumatic fever.

Following this illness he began to notice palpitation and dyspnea on exertion. These progressed through a period of two years, when he was forced to seek hospital aid for several months. Following recovery, tonsillectomy was performed, and he remained well for three years. That winter (five years ago) he suffered an attack of "bronchitis"—cough, blood-streaked sputum and dyspnea—lasting for several months. Similar attacks have occurred each winter since and during one such attack two years ago, the second attack of decompensation occurred. He improved with rest in bed and with the administration of digitalis, which he has been taking off and on ever since, but constant cough, the expectoration of considerable amounts of sputum, dyspnea and edema in the evening have persisted. He has worked irregularly nevertheless up to the present illness.

Five weeks before admission sore throat developed, followed by rapid increase of dyspnea, cough, edema, and weakness. The amount of sputum expectorated increased notably, and became semipurulent in character. Two weeks ago chills and fever began and weakness forced him to bed. His condition slowly became worse until the day before admission a studden, stabbing pain in the left chest, augmented by respiratory effort, forced him to come to the hospital.

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Admission Physical Examination.—Temperature 101° F., pulse 120 at apex, 102 at wrist, both totally irregular. Respiration 42. He was an extremely ill, emaciated, dehydrated man, dyspneic and orthopneic with shallow, labored respirations and a constant cough accompanied by expectoration. There was slight cyanosis and no edema. The veins of the neck were moderately distended. The precordial region bulged, and the apical impulse was diffuse, yet forceful, in the fifth and sixth

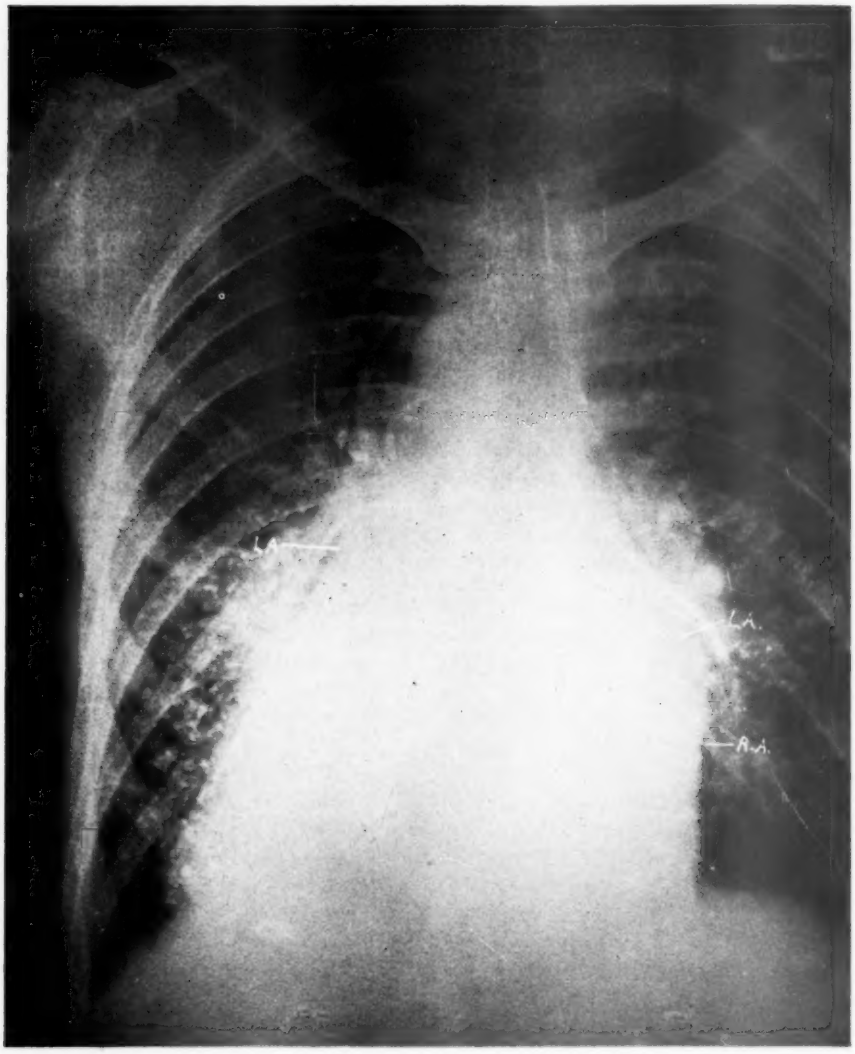

Fig. 1.

left interspaces, 10.5 cm. to the left of the midline. A systolic and a long, rough diastolic murmur were present, the latter best heard in the third and fourth left interspaces to the left of the sternal margin. Limitation of motion over the left lower chest and retraction of the interspaces here were quite apparent. Percussion was normal over the right lung, but posteriorly below the scapula on the left there

was definite dullness. In this region were many fine and coarse moist râles, distant bronchial breathing and increased voice sounds. Elsewhere the respiratory murmur was normal, but râles of various types were heard over the whole chest, though not as numerous as at the left base. The liver was moderately enlarged. There was no ascites.

The urine contained moderate amounts of albumin and many hyaline and granular casts. There were 5,500,000 red blood cells per c.mm. and 15,000 white cells with a moderate increase of the polymorphonuclear leucocytes. The blood urea nitrogen and creatinine were normal. The Wassermann was negative, and blood cultures were negative. No tubercle bacilli were found in several examinations of the sputum, but numerous pyogenic cocci of many kinds were present. The six foot x-ray plate of the chest showed a large heart with enlargement of the curve between the aorta and left ventricle and secondary congestion of the lungs more marked on the left.

The clinical diagnosis was "mitral stenosis, cardiac insufficiency and bronchopneumonia at the left base."

Course.—The day following admission a friction rub appeared in the left axilla and frank tubular breathing was heard posteriorly. He was treated with digitalis, with rest in bed, and was given a sufficient amount of fluid. Steady improvement occurred, although for seventeen days a temperature of from 100° to 102° persisted. The lungs cleared slowly except the signs at the left base. Here impairment of the percussion note and moist râles remained, the breath sounds varied from complete suppression to an amphoric quality. The expectoration of sputum, mucopurulent in character, varied from 150 to 400 c.c. per diem.

After five weeks of these persistent signs the possibility of a unilateral, basal bronchiectasis, secondary to compression of the left main bronchus by the left auricle was suggested. Consequently lipiodol was injected into the trachea, and although evidence of bronchiectasis was lacking, the iodized oil clung rather neatly to the walls of the bronchi, disclosing a surprisingly wayward course of the left main bronchus. The natural downward convexity was disturbed by an upward displacement, beginning a few centimeters from the origin of the bronchus from the trachea, resulting in a somewhat S-shaped curve (Fig. 1). Marked narrowing was also apparent at this point. X-ray plates were then taken during deglutition of a thin barium mixture and these demonstrated a displacement of the esophagus to the right and backward.

Following the lipiodol injection, the patient again ran fever for a few days and was delirious. He soon recovered and was discharged much improved. At present he is still taking digitalis, leading a quiet but comfortable home life, yet cough with expectoration of 50 or 60 c.c. of sputum persists, together with some impairment of percussion and persistance of moist râles at the left base *only*.

COMMENT

The first report of cases of compression of the left main bronchus by an enlarged left auricle was made in 1838 by King.[1] He presented four cases which showed partial collapse of the left main bronchus at necropsy. Three of these were apparently cases of mitral stenosis, while the fourth was that of a child, two and a half years old, with "cerulean blue" cyanosis. The exact type of cardiac lesion is not quite clear. Anomalies of both the tricuspid and mitral orifices were, however, present. Both auricles were much enlarged and compression of a small part of the right main bronchus, as well as the left, had occurred.

In no case did compression reduce the lumen to more than one-half the original size, and King was of the opinion that, for this reason, pulmonary signs are not to be expected during life. He stated that the base of the left lung appeared, however, to contain less air than the right, that the bronchioles were filled with "turgid material" and that the whole base seemed partially solid.

Later in 1867, Friedreich[2] reported a case of high-grade mitral stenosis in a young girl who had "distention" of the lower part of the thorax on the left side and high-pitched inspiration and expiration over the left lung base, particularly near the hilus. These signs had persisted for several years when in 1850 he made the diagnosis of compression of the left main bronchus, four years before her death. The diagnosis was confirmed at necropsy by Virchow in 1854.

In 1889 Taylor[3] reported the necropsy of a boy of sixteen with a history of heart failure of three years' duration, clinically diagnosed mitral stenosis. No mention is made of lung signs. The heart was very large, particularly the left auricle which held eleven ounces of clotted blood. The mitral orifice was but a slit. The left bronchus was markedly flattened in an anteroposterior direction, running posterior to, rather than above, the left auricle. The changes in the lungs were described as follows: "The upper lobe (left) was retracted, showing brown induration. The lower lobe was collapsed—the upper two-thirds being almost airless, the lower two-thirds choked with coagulated blood." The right lung was merely edematous.

Between the time of this report of Taylor's and the beginning of the more careful study by German and Austrian workers, scarcely any mention of this phenomenon can be found. Two references to such condition are noted in English textbooks, however. The first is by West[4] who, very briefly, states that the anatomical relation of the left auricle to the bronchus makes it possible that enlargement causes pressure on the bronchus. The other is found in Allbutt and Rolleston's *System of Medicine* in the article by Sansom.[5] The description here is clear-cut and concise and is therefore quoted:

"The left auricle is occasionally so much dilated as to cause obstruction of the left bronchus and thus lead to a series of morbid changes in the lung which result from its total or partial occlusion. These pass through the stages of hyperemia and edema until the final conditions of collapse and induration are reached." And again, "In an early stage the most important symptom is stridulous respiration, confined to the left side of the chest and sometimes accompanied by fine crepitations at the left base. After a time there is dullness to percussion without much change in fremitus on palpation, the probable explanation of which is, that, although the condensation of the lung, which is going on, ought to exaggerate the fremitus, the diminished lumen of the bronchus interferes with access of sound vibrations. The

respiratory murmur, in this condition, becomes harsh, but stridor masks it. The latest stage shows absolute dullness with total absence of vocal fremitus while the respiratory murmur is obliterated. A considerable degree of retraction may be observed in such cases."

In 1910 Stoerk[6] made a careful study of the anatomical relations of the mediastinal contents, particularly of the relations of the chamber of the heart to the main bronchi. He demonstrated the fact that the left auricle made up the posterior and superior parts of the heart and that the bifurcation of the trachea and main bronchi were in close relation just above it, the left main bronchus normally resting on the upper surface for a short distance.

He took measurements of previous observers, Aeby, von Hovorka and Kobler, concerning the angles of departure of the bronchi from the trachea, confirmed them and incorporated them with his own figures into a final estimation of the normal angle. Then in eight cases of mitral stenosis, he showed that the average of the angle of deviation was increased 30°. The minimal deflection in the group of cases of mitral disease was about that of the maximal in normal individuals. He also noted that compression of the left main bronchus occurred frequently.

Two years later Kahler,[7] by bronchoscopy, demonstrated during life a narrowing of the lumen of the left main bronchus in all of thirteen cases of mitral stenosis obtained for study from Kovac's clinic. In one case it was so marked that on bronchoscopic examination the opening through the compressed area appeared only as a slit-like orifice 2 mm. in width. He also measured from the point of view of bronchoscopy, the upward deviation which occurred. In one of these cases signs of "lung compression" at the left base were noted clinically. Two of these cases came to autopsy, and the compression found by bronchoscopic examination was present. Still more recently, Gabert[8] has confirmed these observations of displacement and compression by x-ray, but makes no statement as to the condition of the lungs. His is the first x-ray diagnosis of upward displacement of the left main bronchus. He photographed the chest in lateral and anteroposterior views, increasing somewhat the ordinary exposures for heart shadows, and was able to trace the air containing main bronchi dimly. It was quite evident that spreading of the bronchi occurred in the cases of mitral disease, when compared to his normal roentgenograms.

Quite recently Shaw[9] dealing with enormous dilatation of the left auricle to the right, mentions the clinical findings of consolidation of the left base and profuse expectoration without comment. Shaw[9] and Bramwell[10] also note some displacement of the trachea to the right in the same type of case. The amount of displacement to the right should be carefully measured, however, before assuming that displacement has occurred, since Kahler[7] noted that in from 57 per cent to 75 per

cent of normal individuals the lower portion of the trachea lies slightly to the right of the midline.

Schrötter[11] discusses a cause of elevation of the left bronchus, remote from the present condition, where effusion into the left chest has occurred. This is probably due, he believes, to the fact that the left lung and components are floated or pushed upward, causing rotation of the trachea and bronchi to the left, and not necessitating a widening of the angle of departure. In his second case, pleural effusion on the right side reversed the process; the right main bronchus was pushed up and the left one was lowered.

SUMMARY

In summary, then, bronchial compression by an enlarged left auricle has been known to occur for nearly a century. It is known also that due to this cause compression does occasionally cause morbid changes in the lung, recognizable clinically. The knowledge of this phenomenon may be of use in explaining persistent pulmonary signs otherwise puzzling. At present I believe that compression and displacement of the left bronchus are much more common in mitral disease than is supposed, but only infrequently are they great enough to give rise to secondary lung changes, such as bronchiectasis, chronic basilar infections, and atelectasis. I hope shortly to show that it may also be demonstrated by x-ray examination when no pulmonary signs exist.

The present case gave no evidence of bronchiectasis by x-ray examination, but the bronchial tree was outlined and the compression and displacement of the left main bronchus were apparent. This explains readily the persistence of the expectoration of sputum and of the abnormal pulmonary signs at the left base alone.

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THE EXTRACARDIAL NERVES—III*

Further Observations Upon the Relation of the Extracardial Nerves to Heart-Block

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IT WAS found that accelerator nerve section caused circulatory failure if complete heart-block was present the location of which was in the ventricle, and that stimulation of the accelerator nerves prevented this.[1] Some other effects of extracardial nerve activity associated with these experiments and some minor problems related to them were considered of sufficient interest to report. The experimental conditions were like those of the previous report.

Effect of Accelerator Nerve Stimulation Upon the Heart Rate.—The effect of accelerator nerve stimulation upon the auricles was similar to that which occurs in the presence of the normal sinus rhythm (Table I). The effect upon the ventricles was an increase in the visible tone and force of contraction for a short time following the stimulation, and the action of the two nerves in this regard was the same. No increase in the ventricular rate followed the stimulation of either nerve as is the case in the intact heart, although the other characteristic effects of accelerator nerve stimulation were very striking. (Fig. 1.)

Table I

NO.	RATE BEFORE	AFTER STIMULATION RT. NERVE	OF L. NERVE
	A V	A V	A V
19	130/40	ineffective	172/42
20	120/56	220/56	200/56
58	139/39	200/40	170/40
62	140/56	300/56	240/56
63	140/39	200/40	200/40

Hering[2] and also Daly and Starling[3] obtained an increase in the rate of the ventricle by accelerator nerve stimulation in the dog and cat. Cullis and Tribe,[4] however, have also found that the sympathetic action on the ventricle was much reduced or absent (rabbit heart), although the usual auricular effect was produced. In many experiments a slow decline in ventricular rate was present, but accelerator nerve stimulation did not increase the ventricular rate above that just preceding the stimulation. For example, in one of the experiments, after the production of the block, the ventricular rate was 55

*From the Laboratory of the Faculty of Medicine in Paris.

per minute. Accelerator nerve stimulation did not increase it
A V
(215/55). Fifteen minutes later the ventricular rate was 39 per min-
A V
ute and accelerator nerve stimulation did not affect it (200/40). In three animals in which there was an excessive amount of accelerator

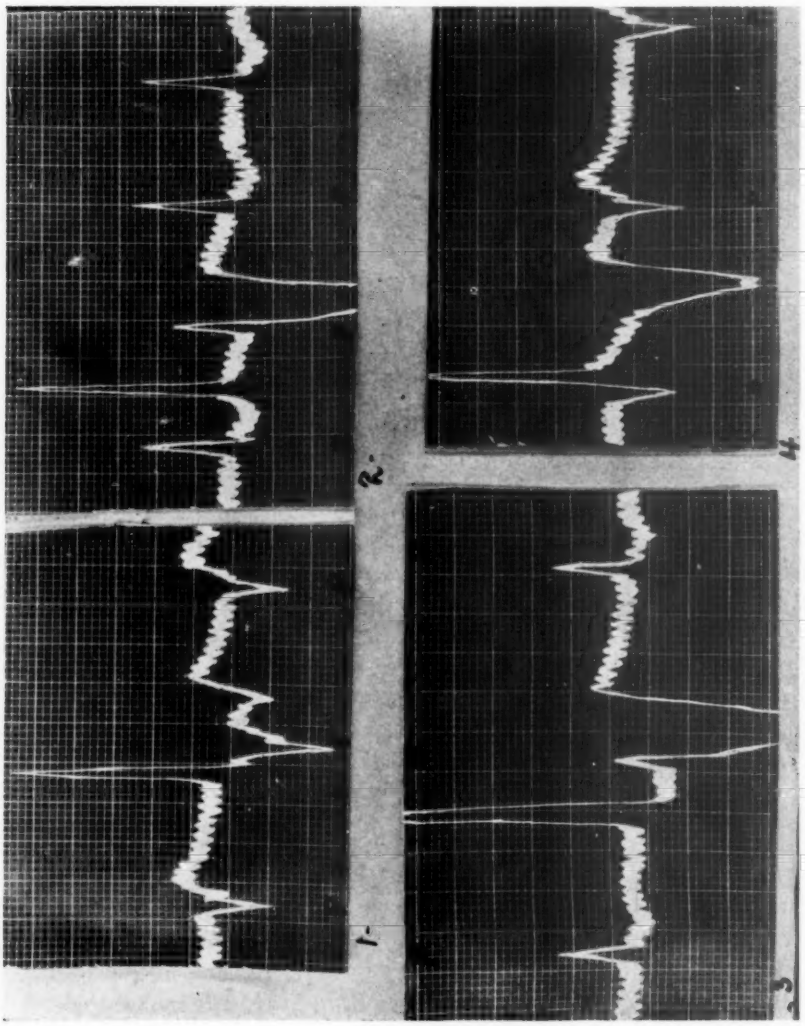

Fig. 1.—The effect of accelerator nerve stimulation in complete block. Axial (R.A.-L.L.) leading. Time in fiftieth seconds. (1) Auricular rate 152. The P-wave is inverted and followed by a positive P-T. This was constant during the half hour which preceded. (2) Just after stimulation of the right accelerator nerve. Auricular rate 190. The P-wave is positive, high, and followed by a negative P-T. Note the exaggerated effect upon the T-wave. (3) Ten minutes later. The auricular rate is 125. The other effects of accelerator nerve stimulation still endure. (4) After stimulation of the left accelerator nerve. The auricular rate is 125. The P-Wave is again negative. The negativity of the T-wave is greatly lessened.

nerve stimulation a gradual rise of the ventricular rate appeared which did not exceed the ventricular rate present at the beginning of the experiment. An illustration of this is the following—in one of the
A V
dogs after the production of the block the rate was 130/45 and thirty
A V
minutes later it was 130/24. Following ten minutes' stimulation of

both accelerator nerves the highest ventricular rate obtained was forty-five per minute. Whether this slow rise in the rate was caused by the prolonged increase in the auricular activity rather than the direct effect of the accelerator nerves upon the ventricles could not be determined from these experiments.

The Effect of Adrenalin Upon the Block.—Adrenalin (0.1-0.2 c.c.) intravenously always resulted in the onset of ventricular fibrillation when it was administered in the presence of complete block. Small doses had no effect upon the ventricular rate.

The Electrocardiogram.—The electrocardiographic changes induced by accelerator nerve stimulation in complete block were similar to those which occur in the intact heart.[1] Right nerve stimulation caused increase in the height of the P-wave or if it was negative, caused it to become positive, and the left nerve stimulation usually caused inversion of the P-wave. (Fig. 1.)

The effect of the two nerves upon the T-wave was difficult to compare because the accelerator nerve stimulation very frequently altered the form of the QRS complex; and the T-wave changes induced were exaggerated and of long duration.

It appeared, however, as if the changes which accelerator nerve stimulation caused in the form of the ventricular curve were of the same character as those in the intact heart, stimulation of the left nerve tending to force the T-wave upward, and stimulation of the right nerve tending to force the T-wave downward, i.e., the effect of stimulation of each accelerator nerve upon the form of the electrocardiogram was qualitatively similar to that occurring in the intact heart. (Fig. 1.)

The Relation Between Vagus Stoppage and the Heart-Block.—The pre-automatic pause and the rhythm of development were constant in each heart and did not alter with the repetition of the block if recovery occurred. In one instance, recovery and reinduction of the block occurred seven times, and the length of the pre-automatic pause and the rhythm of development did not change. This was also the case after the accelerator nerves had been sectioned.

The duration of the stoppage of the intact heart induced by stimulation of the right vagus nerve was approximately equal to the length of the pre-automatic pause after complete block was established. When escape from stimulation occurred early, i.e., the duration of the stoppage was short, the pre-automatic pause was also short, and the onset of idioventricular rhythm was spontaneous and the rhythm of development was rapid. If no escape occurred during long stimulation of the right vagus nerve, the pre-automatic pause when the block was induced was always so long that rhythmic tapping of the ventricle had to be employed to hasten the onset of the idioventricular rhythm. This relation between the vagus nerve and the pre-automatic

pause has been observed by Erlanger and Hirschfelder.[5] When differences appeared between the duration of heart stoppage from vagus stimulation and the duration of the pre-automatic pause, the difference was one that favored the pre-automatic pause, i.e., the duration of vagus stoppage was less than the pre-automatic pause, which can be explained by the fact that stoppage of the heart from stimulation of the vagus nerve is broken by the autonomy of one of the points for impulse production, viz.—the S-A node, the A-V node, or the ventricles. Since the inherent rhythmic frequency of the first two is greater than that of the ventricles, the escape from vagus stimulation occurs sooner when it arises at either of these two points. Hence differences ought to be in the nature of a longer pre-automatic pause than vagus stoppage, which actually is the case.

There also was an inverse relation between the duration of heart stoppage during right vagus nerve stimulation and the time required for the appearance of the circulatory failure which followed the accelerator nerve section. Whenever the vagus effect was intense, there was a constant tendency for the time before death occurred following accelerator nerve section to be considerably shorter than where the escape of the heart from vagus stimulation was very prompt, differences arising so great as fifteen minutes for the one as against fifty minutes for the other.

Vagus Nerve Stimulation in Heart-Block.—The effect of vagus nerve stimulation upon the auricles was the same as that before the production of the heart-block, and no effect upon the ventricles directly attributable to the vagus nerve stimulation was observed. It was common to observe an after-effect of stimulation, an increase in the rate of the auricle and an increase in the tonus and strength of contraction of the ventricle. This was due to the sympathetic fibers which descend in the vagus trunk. It is of interest to note that the rhythmic stimulation of these fibers (by rhythmic stimulation of the vagus trunk after full doses of atropin) prevented the onset of the circulatory failure which appears after accelerator nerve section.

The Effect of Intact Vagi in Heart-Block When the Accelerator Nerves Are Sectioned.—In three animals the vagi were intact, and complete block was induced. In these the only effect of section of the vagi nerves was a small increase in auricular rate. In two other animals in which the vagi were intact, and block was induced, the accelerator nerves were sectioned. No difference in the usual effect occurred and circulatory failure ensued. Hence, the tonic activity of the sympathetic fibers which are contained in the vagus nerve trunk were not sufficient to prevent the circulatory failure and death which results from the accelerator nerve section, although strong and frequent excitation of these fibers did so.

The Relation Between the Ganglia Stellata and Rami Communicantes.—Singer[6] has studied the afferent (sensory) pathway for the nerves supplying the pericardium, the epicardium, and the first part of the aorta and has found that the reflex reaction to the stimulation of these parts is obliterated by the section of the n. rami communicantes of the C_8D_{1-3} spinal nerves. He has recommended the section of these nerves for the relief of cardiac pain as the alternative to removal of the stellate ganglia upon the ground that the afferent pathway only is broken. In three animals, after block was induced, the rami communicantes to these nerves were sectioned. The main sympathetic nerve trunk and the ganglia stellata were intact. There was no difference in the effects from those which occur when the ganglia stellata are removed. This suggests that the efferent (motor) pathway for the accelerator nerve is probably the same (n. ram. comm. C_8D_{1-3}) and that in so far as choice of operation is concerned no physiological distinction can be made between the resection of the ganglia stellata and the section of the n. rami communicantes C_8D_{1-3}.

SUMMARY

1. The effect of accelerator nerve stimulation upon the ventricular rate in complete block was found to be insignificant, although its action upon the form of the electrocardiogram is marked.

2. Adrenalin administered in the presence of experimental block caused ventricular fibrillation.

3. There is a relation between the effect of stimulation of the right vagus nerve, the pre-automatic pause of the ventricles and duration of life of the heart after accelerator nerve section.

4. The tonic activity of the sympathetic nerve fibers contained in the vagus trunk was insufficient to support the circulation in the presence of accelerator nerve section although stimulation of these fibers did so.

5. Section of the n. rami communicantes C_8D_{1-3} has the same effect as the removal of the stellate ganglia.

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THE EXTRACARDIAL NERVES—IV*

An Experimental Study of Coronary Obstruction

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INTRODUCTION

ALTHOUGH accelerator nerve section does not significantly affect the changes which follow many types of injury to the heart,[1] the important practical aspects of coronary closure suggested that it would be of interest to determine its relation to the extracardial nerves. The points investigated were the effect of accelerator nerve section and vagus nerve stimulation upon the closure of the coronary sinus and large and small arteries, and the associated electrocardiographic changes. Some of the observations included, although not directly concerned with the problem stated, are closely associated with it. Experimental studies upon the effects of coronary obstruction have been made by Lewis,[2] Smith,[3] Gold *et al.*,[4] and others. Danielopolu and Marcu[5] also studied the relation between the closure of coronary arteries and the accelerator nerves and have found that accelerator nerve section exaggerates the changes induced by closure of coronary arteries.

METHOD

The experiments were made upon dogs with chloretone narcosis, vagus nerve section, artificial respiration, opened chest and artificially maintained temperature. Axial electrocardiographic leading (R.A.-L.L.) was employed and where it was considered of interest other leads (R.A.-L.A. and L.A.-L.L.) were added. In twelve experiments the coronary sinus was ligated or clamped at the coronary dimple, before it opens into the cavity of the right auricle. After the accelerator nerves were sectioned there was an interval of one hour before the ligation. This length of time was suggested by other observations.[1] In the control animals the accelerator nerves were intact but the same interval was also allowed before the ligation. The same procedure was followed with the ligature of the arteries in 24 experiments.

RESULTS

Coronary Sinus.—The ligation of the coronary sinus did not completely obstruct the venous flow because of the venii Thesbesii, and occasionally this compensatory venous bed was large enough to allow a coronary circulation which prevented the death of the heart during the period of the experiment.

The immediate effect of the ligation of the coronary sinus was marked engorgement of the large veins and the appearance of many others not previously visible. This was followed by intense cyanosis

*From the Laboratory of Physiology, Faculty of Medicine, Paris.

of the surface of the left ventricle which did not, however, spread further anteriorly than the interventricular groove until death was imminent. The left ventricle enlarged and appeared functionless, hanging like a distended sac from the contracting portion of the heart, whereas the right ventricle retained its function and good color. At some time after the ligation (which varied from ten to fifty minutes), incomplete heart-block appeared. It was most often cyclic, i.e., it appeared first as a very high degree of block which passed into 2:1 block and it was then followed by 1:1 beating (recovery); and it slowly and irregularly repeated this cycle until death occurred. The auricle maintained its regular rhythm throughout and it suffered little alteration in its rate. No tachycardias and very few premature beats appeared during the course of the changes which finally resulted in death.

Post-mortem, the muscle of the external wall of the right ventricle was soft, whereas that of the left ventricle felt hard to the touch and was thicker than normal, and the cut surface oozed blood upon section. It was dark in color, and presented an appearance not unlike that which is seen with chronic passive congestion. The endocardial surface of the left ventricle including the septal wall was a purplish hue and appeared edematous, but that of the right ventricle including the septal wall was normal in color and appearance. The congestive discoloration extended into the septum about half-way through its thickness.

The Electrocardiogram.—The electrocardiogram of the axial lead presented an elevation of the T-wave. This positive effect upon the T-wave, although it occurred constantly, varied greatly in amount and time of onset, and no parallel existed between the electrocardiographic and the other changes occurring in the heart, since effects varied from an exaggerated early electrocardiographic change with delayed death to minor electrocardiographic change with early death (Table I). In two instances the R-T fusion appeared as the effect of the ligation (Fig. 1).

TABLE I

DOG	TIME BEFORE ECG CHANGE APPEARED	THE DEGREE OF CHANGE IN ECG	DEATH	ACCELERATOR NERVES
I	2 min	marked	15 min.	cut
II	3 "	"	50 "	"
III	15 "	"	25 "	"
IV	60 "	small	65 "	"
V	3 "	marked	21 "	"
VI	10 "	small	60 "	"
VII	3 "	marked	15 "	intact
VIII	5 "	"	35 "	"
IX	3 "	small	31 "	"
X	5 "	marked	no death	"
XI	no ECG		5 min.	"
XII	" "		no death	cut

There was no relation present between the heart rate, the effect of stimulation of the right vagus nerve and the effects of the ligature. The effect of accelerator nerve stimulation upon the altered electrocardiogram which the ligature induced was the same as under other conditions,[6, 1] right nerve stimulation lessening the height of the T-wave and left nerve stimulation increasing the height of the T-wave.

The Effect of Accelerator Nerve Section.—Accelerator nerve section did not influence the resistance of the heart to the effects of the ligature. Early death was equally common following the ligature when the accelerator nerves were intact as when they were sectioned and as many instances (one) in which the heart survived the ligature of the coronary sinus occurred when the nerves were sectioned as when they were intact. The nerve section did not influence the cyclic heart-block nor did it appear to effect the electrocardiographic changes which followed the ligature of the coronary sinus. The only effect

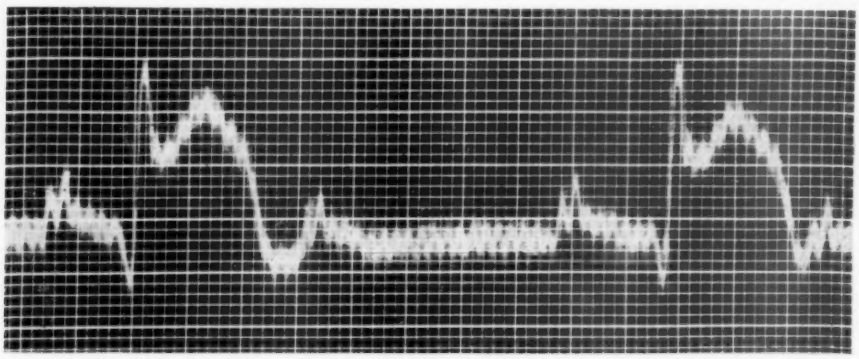

Fig. 1.—Axial (R.A.-L.L.) ECG. Time in fiftieth seconds. Ligature of the coronary sinus. A 2:1 heart-block and the RT fusion are present.

observed from the accelerator nerve section was in the manner by which the death of the heart occurred. When the accelerator nerves were intact, death occurred by the sudden onset of ventricular fibrillation. If the accelerator nerves were sectioned one hour before the ligature, the death occurred by diastole; i.e., a gradual dilatation of the right ventricle with a decrease in the muscle tone and strength of contraction.

Ligature of Coronary Arteries.—Twenty-four experiments were made. In all instances, shortly after the ligation, visible evidence of the effect appeared as a sharply demarcated discoloration of the area of heart muscle supplied by the branch ligated, associated with loss of function.*

Effect on Rate and Rhythm.—The ligature of small vessels caused no changes in the rate or rhythm but the ligation of large vessels

*A more detailed description of the events which follow coronary ligature is given by Lewis.[2]

caused a decline in the heart rate and was often followed by sudden variations in the rate which were phasically recurrent. The electrocardiograms were inconstant; some showed no alteration in the P-wave or P-R interval, other showed alteration in the form of the P-wave. These changes were probably related to the alterations of

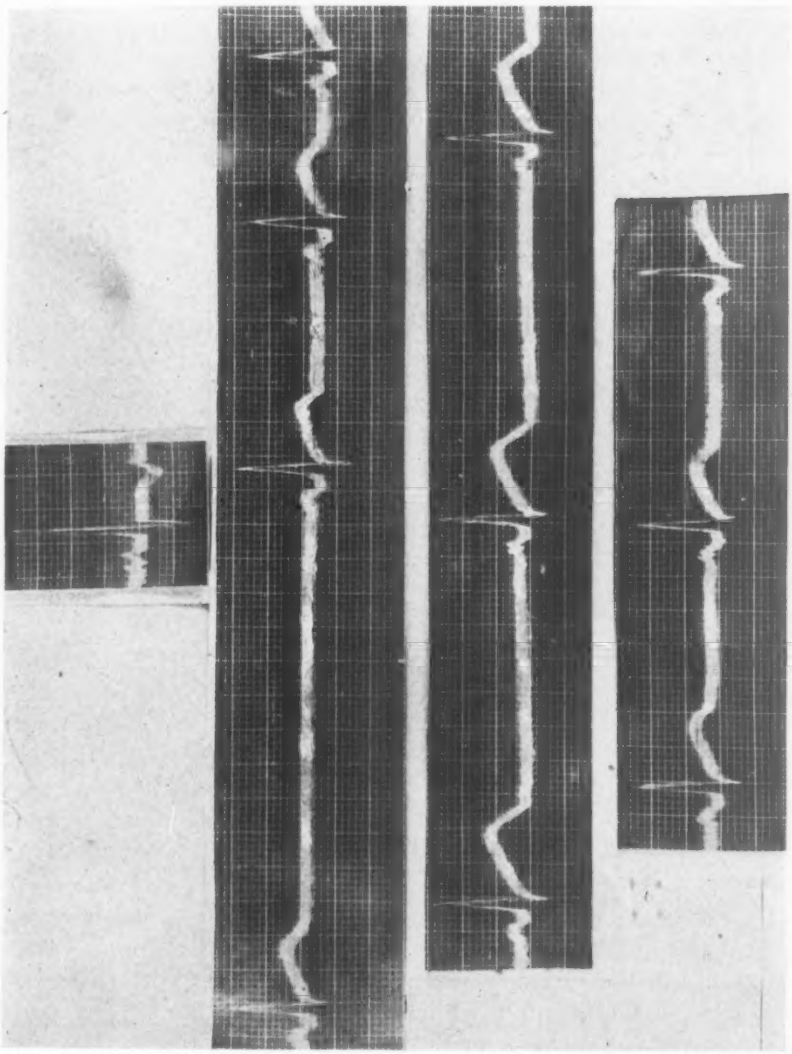

Fig. 2.—Axial (R.A.-L.L.) ECG. Time in fiftieth seconds. Ligature of the artery to the S-A node. (1) The normal sinus rhythm. (2) Complete irregularity in the rhythm which was the first effect of the ligature. (3) During a period of slow and regular rhythm (a slow phase). (4) During a period of more rapid and regular rhythm (a rapid phase).

the blood supply to the S-A node, since similar phasic variations in the rate of the auricles were observed after ligature of the artery to the S-A node (Fig. 2). They were also very common during the course of the heart failure which followed accelerator nerve section in heart-block,[1] and were occasionally observed to occur after section of all the extracardial nerves in the intact heart. These observations

suggest that nonrespiratory sinus arrythmia and sinus block are the effect of conditions which diminish the blood supply to the S-A node.

Ventricular premature beats were numerous and often recurred in groups. Lewis[2] noted that they appeared within from three to five minutes after the ligation in 7 of 17 animals. In these experiments they appeared later. The electrocardiographic form they assumed was mostly that of the right ventricular premature beat after ligation of the right coronary artery and of the left ventricular premature beat after ligation of branches of the left coronary artery.* Smith[3] has also noted the appearance of left ventricular premature beats after ligature of the descending division of the left coronary. Tachycardia was rare and it occurred in two of the twenty-four dogs; in one instance it was left ventricular tachycardia and followed ligation of the entire left coronary artery, ending with ventricular fibrillation. The other was nodal tachycardia, of short duration and irregularly recurrent

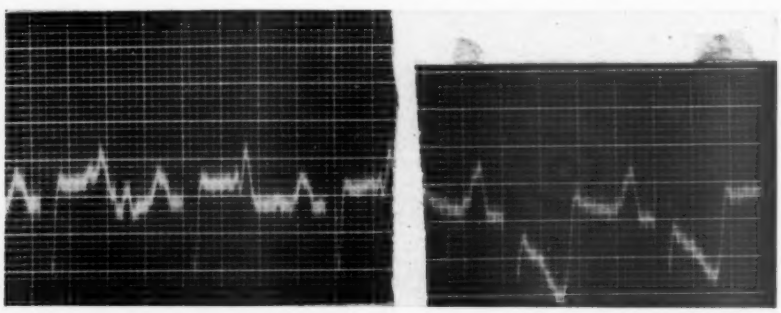

Fig. 3.—Axial ECG. (R.A.-L.L.) Time in fiftieth seconds. (*1*) Before ligation of the right coronary artery. (*2*) Ligature of the right coronary artery (ST fushion).

during the course of the experiment. It appeared after the ligation of the largest branch of the circumflex division of the left coronary artery.

The Electrocardiogram.—The ligation of the right coronary artery forced the T-wave of the electrocardiogram downward with a loss of the RT interval, and caused the ST fusion (Fig. 3). The ligation of the left coronary arteries forced the T-wave of the electrocardiogram upward with loss of the RT interval (Fig. 4, *a* and *b*). As in the case of the ligature of the coronary sinus, effects were constant in character but varied in the degree to which they occurred.

The RT fusion phenomenon was an inconstant occurrence after the closure of the left coronary artery. This has also been the observation of Gold *et al.*,[4] and others. However, the ligation of the second large branch arising from the circumflex division of the left coronary

*Concerning the question of interpretation of the electrocardiographic form of the premature beats, right and left, or basal and apical, either may be applied since the distribution of the right coronary artery is both to the right and basal portion of the heart and the left coronary artery, particularly its anterior division to the left and apical portions of the heart.

artery almost constantly resulted in the appearance of this form of electrocardiogram (Fig. 5). It supplies the external wall of the left ventricle on the posterior surface of the heart just above and to the right of the cardiac apex. When it failed to appear, the additional ligation of other branches from the branches of the anterior or circumflex divisions of the left coronary artery which may also supply this portion of the heart induced its appearance (Fig. 4).

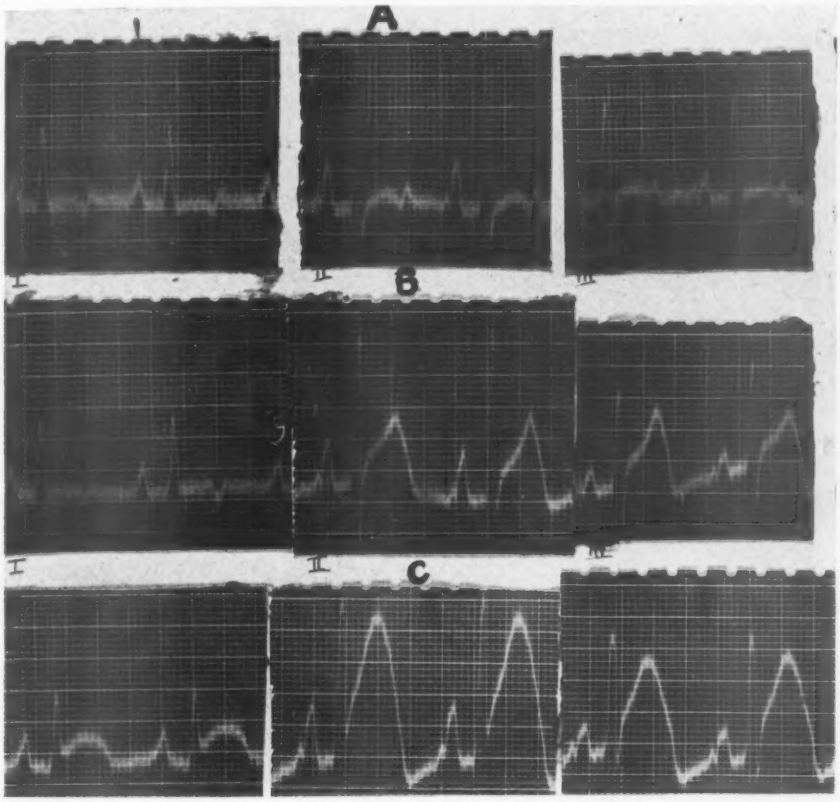

Fig. 4.—Electrocardiograms R.A.-L.A.; R.A.-L.L.; L.A.-L.L.; derivations I, II, III. Time in fiftieth seconds. *A*, Normal. *B*, Ligature of the first branch and part of the second branch from the circumflex division of the left coronary artery. *C*, Ligature of a branch from the anterior division of the left coronary artery which also supplies this area.

Accelerator nerve stimulation had the same effect upon these electrocardiograms as upon the normal.[1, 6] Stimulation of the right nerve exaggerated the changes produced by closure of the right coronary artery and stimulation of the left nerve lessened them, causing the curve to approach the original form. Stimulation of the nerves in the presence of closure of left coronary vessels had the reverse effect, i.e., right nerve stimulation lessened the change and left nerve stimulation increased it.

Effects of Accelerator Nerve Section.—When the accelerator nerves were sectioned one hour before ligation, death occurred in a manner similar to that which occurred after ligature of the coronary sinus with the accelerator nerves sectioned, with dilatation and diminishing strength of contractions until standstill occurred. After this, ventricular fibrillation could very frequently be produced by faradization of the accelerator nerves. The ventricular fibrillation did not include the infarcted areas.* When the accelerator nerves were intact, death occurred by the onset of ventricular fibrillation. When the accelerator nerves were sectioned immediately before the ligature, death occurred by the onset of ventricular fibrillation whenever the time for the death to occur was short, otherwise the diastolic type of circulatory failure resulted. This was the single constant difference observed between the hearts in which the accelerator nerves were sectioned and

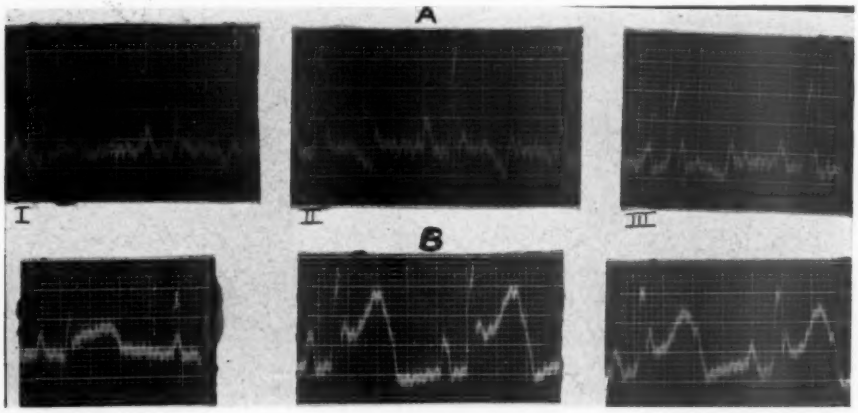

Fig. 5.—Electrocardiograms corresponding to derivations I, II, III. Time in fiftieth seconds. *A*, Normal. *B*, Ligature of second branch from the circumflex division of the left coronary artery (RT fusion).

those in which they were intact. No differences were observed in the time for the death to occur, in the resistance of the heart to the amount of the coronary arterial supply ligated, in the alterations in the rate or rhythm following the ligation, or in the amount of irritative phenomena (premature contraction or tachycardia) which appeared. It has already been mentioned that Danielopolu and Marcu[5] have observed significant changes to follow accelerator nerve section in the presence of coronary obstruction.

The Vagus.—There was no relation between the effect of maximum stimulation of the right vagus nerve and the amount of arterial ligature required to induce circulatory failure. There was a constant tendency, however, for the number of premature contractions which appeared after the ligation to be less numerous when the response to

*This has been described by Garrey[7], Lewis[2], Gold[8] and others.

vagus stimulation was marked. In order to test this further, the effect of prolonged vagus stimulation was tried in 8 other dogs, using faradic stimulation of the right vagus nerve in 4 and pilocarpine in large doses in the remainder, and it was found that the number of premature contractions was greatly diminished when compared to the number which followed coronary artery ligature under the same conditions without vagus stimulation, since in 6 of these animals very few premature contractions occurred, and in the other 2, although many appeared, the effect, when compared to the effect of ligature in hearts which presented a similar vagus reaction (very short stoppage time and a rapid rate of escape) also showed diminution in the number of premature contractions occurring.

SUMMARY AND CONCLUSIONS

1. The changes which follow closure of coronary vessels (arterial or venous) in the dog are not altered by section of the accelerator nerves except in the manner by which the death of the heart occurs. When the nerves are intact, death occurs by the onset of ventricular fibrillation and when they have been sectioned for one hour previously, death occurs by dilatation and diastole.

2. A diminished blood supply to the S-A node is suggested as the cause of nonrespiratory sinus arrhythmia and sinus block.

3. The electrocardiographic form of the premature beats which appear after closure of coronary arteries tends to follow the anatomical distribution of these vessels, since the closure of the left coronary arteries causes the appearance of premature beats, left ventricular in form, and the closure of the right coronary artery premature beats—right ventricular in form.

4. Closure of the right coronary artery causes negativity of the T-wave and the appearance of the ST fusion and the closure of left coronary vessels causes positivity of the T-wave and also the appearance of the RT fusion when the posterosuperior portion of the cardiac apex is thrown out of function.

5. Strong vagus nerve stimulation causes diminution in the number of premature contractions which occur as a result of coronary ligature.

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ABNORMALLY LONG PAPILLARY MUSCLES OF THE HUMAN HEART*

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ORDINARILY the papillary muscle of the human heart is attached to the valve leaflet by a number of fibrous chordae tendineae which are almost as long as, or even longer than, the muscle. Occasionally, however, macroscopic muscle bands extend upward into these cords and may even traverse their whole length, or more rarely, the papillary muscle itself may replace several chordae tendineae and be attached directly to the valve.

In the literature I have been able to find only two references to such anomalies, although they must certainly occur in the experience of every pathologist whose material from necropsies is abundant. In 1896 Przewoski described four cases. In three cases the tip of the normal papillary muscle in the left ventricle was prolonged into a thin extension which took the place of a cord. This form of the anomaly he did not consider altogether rare. He pronounced his fourth case to be more unusual; in this, a large anterior papillary muscle sent out a large muscular extension which entirely replaced several chordae tendineae and was inserted into the ventricular surface of the mitral valve up to the fibrous ring. Przewoski laid down the criterion that only the papillary muscles whose tip extended up to the valve should be considered abnormally long.

In 1910 Orsós-Pécs described twelve cases of anomalies of this type and mentioned another. In four of the described cases a cylindrical muscular beam from the anterior papillary muscle was inserted into the posterior leaflet of the tricuspid valve up to the attachment of the cusp. The lamella of insertion was relatively large. In the other eight cases muscular beams from the anterior papillary muscle of the left ventricle were inserted in the ventricular surface of the anterior leaflet of the mitral valve. When the muscle bundle was inserted into the middle of the valve leaflet, the plate of insertion was symmetric and triangular. When the bundle originated from the right side of the anterior papillary muscle, it fused with the corresponding part of the anterior cusp with a spade-shaped lamella of insertion which turned laterally and eventually connected with the ventricular wall. Orsós-Pécs explained the fact that the lamella of insertion of these bundles in the right ventricle always ended at the attached edge of the valve on the basis that the venous orifice of the right ventricle

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is bounded entirely by muscle, while in the left venous orifice the muscle over the anterior valvular cusp is missing. One of his patients was the son of another patient reported, a circumstance which argued that the anlage might be hereditary. In one case there was a calcified plaque at the point of insertion and in another on the auricular side of the point of insertion of the muscle bundle was a subendocardial tubercle. Orsós-Pécs thought these features could be explained by the stress of abnormal pull of the muscle.

I have found five cases of anomalies of this type. These occurred in about 550 necropsies, an incidence of 0.91 per cent.

Fig. 1.—(Case 1) Left anterior papillary muscle is inserted directly into the anterior cusp of the mitral valve just beneath the noncoronary cusp of the aortic valve.

REPORT OF CASES

CASE 1.—The subject was a man, aged sixty years, who died from uremia following an acute exacerbation of chronic pyelonephritis. The systolic blood pressure was 220 mm. and the diastolic, 110 mm. The heart weighed 476 gm. (body weight, 61.4 kg., or 135 pounds). There was coronary sclerosis graded 2. With the exception of moderate hypertrophy, moderate coronary sclerosis and the anomaly, the heart appeared normal. The anterior papillary muscle of the left ventricle was 5.0 cm. long on its free inner surface and 2.5 cm. long on its mural surface (Fig. 1). It was 1.6 cm. broad at its base, which was formed by several fused trabeculae

carneae. From its base it tapered gradually upward into the ventricular surface of the anterior leaflet of the mitral valve with which it fused, extending in the valve to within 0.3 cm. of the line of attachment of the cusp to the membranous septum beneath the noncoronary cusp of the aortic valve. At its upper extremity it was 0.5 cm. broad and quite flat. From the posterior and lateral aspects of the papillary muscle the usual chordae tendinae were given off and were attached to the valve leaflets in the usual manner. One of the chordae tendineae was rather thick in its upper portion, but there was no evidence of preexisting endocarditis unless this thickened strand might be so considered. The posterior papillary bundles were of the usual form. The functional capability of the mitral valve was apparently normal.

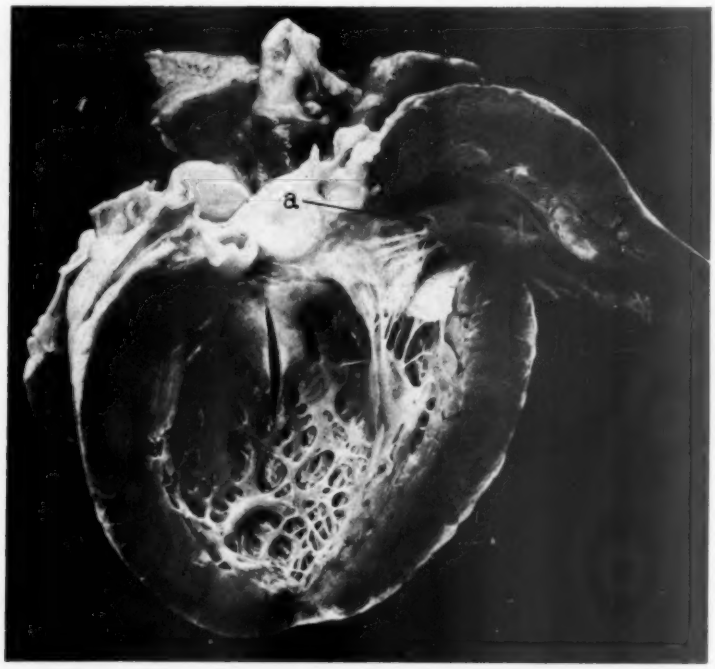

Fig. 2.—(Case 2) The large left anterior papillary muscle comes to a point at the margin of the anterior cusp of the mitral valve. The apex, *a* is attached directly to the valve and short chordae tendineae are given off laterally from the muscle bundle.

Case 2.—The subject was a woman, aged forty-nine years, who died of cardiac decompensation following hypertension. The heart weighed 744 gm. (body weight, 73 kg., or 160 pounds). The left ventricle was considerably hypertrophied and dilated and the right ventricle was moderately hypertrophied and much dilated. The large anterior papillary muscle of the left ventricle was formed mainly by fusion of three trabeculae carneae, the middle muscular projection being the largest (Fig. 2). Above and on the right side the fused bundles came to a blunt point, 0.2 cm. broad, which was inserted into the free edge of the anterior leaflet of the mitral valve near its extreme right end, but the muscle did not penetrate far into the leaflet nor connect with the vetricular muscle. The insertion was more tendinous than muscular. Chordae tendinae, which were shorter than usual, arose from the sides of the papillary muscle and were inserted into the valve leaflets normally.

In this case the muscular attachment of the papillary muscle held the right end of the anterior leaflet in a rather fixed position, so that regurgitation would perhaps have been more marked if the mitral ring had become dilated.

CASE 3.—The subject was a man, aged twenty-nine years, who died of electric shock. The heart appeared normal except for a few subepicardial petechiae. The left anterior papillary muscle consisted of one large, cone-shaped bundle with two smaller ones on the left and an anomalous bundle above and on the right (Fig. 3). The latter was connected with the main papillary muscle by narrow cords of muscle and with trabeculae carneae medial to it. It tapered as it ascended and was inserted into the ventricular surface of the anterior cusp of the mitral valve into which it extended halfway to the membranous attachment of the cusp close to its right side. It then connected with the muscle of the wall of the ventricle. Near

Fig. 3.—(Case 3) Anomalous muscle bundle, *b*, associated with the left anterior papillary muscle is inserted into the anterior cusp of the mitral valve.

the valve it sent off a small cylindrical beam of muscle upward and to the right which also joined the muscle of the wall of the ventricle. The lamella of insertion of the anomalous bundle was 0.4 cm. wide.

CASE 4.—The subject was a man, aged thirty-eight years, who died of pulmonary complications following gastroenterostomy for duodenal ulcer. The mitral valve showed acute vegetative endocarditis. A number of chordae tendineae of the posterior papillary muscle of the left ventricle contained cylindrical bands of muscle which extended as far as the insertion of the cords into the mitral leaflets (Fig. 4). The most lateral muscle bundle of the papillary muscle gave rise to a muscular beam, 0.2 cm. in diameter in the middle, which extended into the posterior cusp of the mitral valve, becoming thicker as it approached the valve. It contained some tendinous strands and at the upper extremity divided into two main muscular

beams and several small chordae tendineae. At about the middle it had a small muscular beam connecting it to one of the trabeculae carneae of the wall of the ventricle.

CASE 5.—The subject was a boy, aged fourteen years, who died of suffocation due to inhalation of food into the bronchi. The heart was somewhat hypertrophied, weighing 271 gm. and both ventricles were considerably dilated. On the anterior wall of the right ventricle was the usual large papillary muscle, but instead of having the common attachment of chordae tendineae to the adjacent halves of the medial and anterior cusps of the tricuspid valve it passed directly up under the ventricular surface of the anterior cusp (Fig. 5). It gave off a few chordae

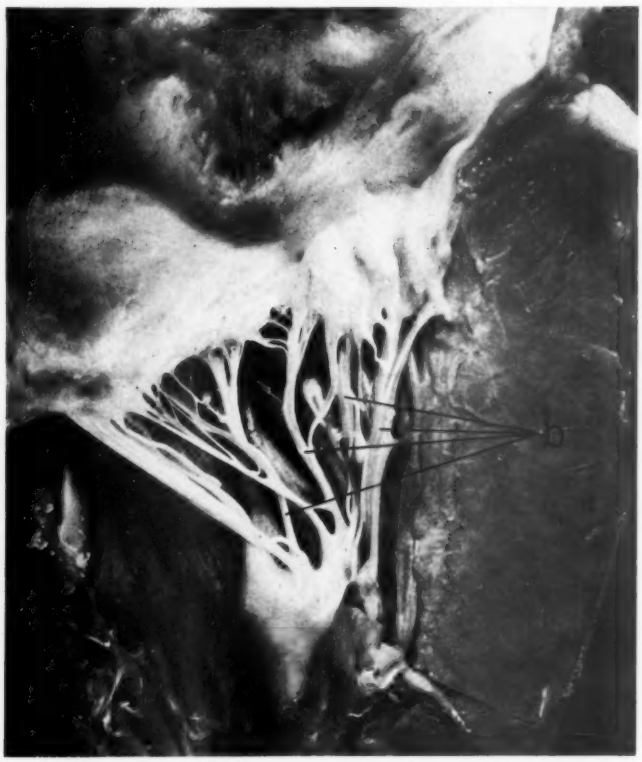

Fig. 4.—(Case 4) Muscle bundles, *b*, are in the chordae tendineae of the left posterior papillary muscle traversing the whole length and extending to the mitral cusps, especially the posterior.

tendineae and became a flat lamella, 0.7 cm. wide, which was inserted in a straight line into the fibrous cusp, 0.55 cm. from the attachment of the valve; several strands of muscle could be seen by transillumination of the cusp passing from this line of insertion to the muscle at the attached edge of the valve. The free portion of the papillary muscle was 2.7 cm. long. Just to the left side of this papillary muscle was a small one which had chordae tendineae attached to the adjacent edges of the medial and anterior cusps of the tricuspid valve but which also sent a narrow muscular lamella up under the valve to be inserted by a flat triangular enlargement into the cusp near its line of attachment; between this triangular lamella of insertion and the papillary muscle proper was a small fibrous area in which muscle

was not visible macroscopically. On the right side of the main papillary muscle was another small papillary muscle, the chordae tendineae of which were attached to the adjacent edges of the medial and posterior cusps of the valve. Several very small papillary muscles gave rise to chordae tendineae which were attached to the posterior cusp.

COMMENT

This type of anomaly is undoubtedly congenital. Early in the development of the atrio-ventricular valves muscular tissue from the myocardium invades the endocardial tissue of the cusps and replaces it. The muscular tissue of the cusps becomes closely blended with the

Fig. 5.—(Case 5) The papillary muscles of the right ventricle (retouched) are cut loose and turned upward to expose their ventricular surfaces. The large papillary muscle, *b*, is inserted into the anterior cusp of the tricuspid valve. The smaller papillary muscle, *b'*, also has a muscular lamella of insertion.

subjacent musculature of the walls of the ventricles. This stage in the development of the cusps is soon followed by replacement of the muscular tissue by collagenous connective tissue, the process evidently taking place mainly from above downward. The subjacent trabeculate musculature also is replaced by collagenous connective tissue. The fibrous cords so developed are the chordae tendineae. Muscular tissue persists at the parietal ends of the cords and forms the papillary muscles. In cases such as those just described the replacement by collagenous connective tissue ceases too soon or is imperfect, and muscular tissue is left in place of chordae tendineae.

The only other explanation would be that localized endocarditis had produced thickening and retraction of the chordae tendineae, causing the cusp of the valve and the papillary muscle to be drawn together. All the facts, however, are opposed to this conception and point rather to the developmental origin of the condition.

The instances of this anomaly previously reported and those described in this paper have not appeared to possess any clinical significance. In Case 2 of this series it seemed that the condition might have increased the insufficiency of a dilated mitral ring had such been present, but the mitral orifice was apparently not very incompetent.

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THE RELATION OF THE WEIGHT OF THE HEART TO THE WEIGHT OF THE BODY AND OF THE WEIGHT OF THE HEART TO AGE*

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WHAT is the normal weight of the human heart? What are the upper and lower limits of normal? Which weights should be considered normal and which abnormal? Just where is the line to be drawn between the normal and the abnormal? The literature is at variance on the subject of just what constitutes the normal or average weight of the human heart and it contains little, if any, information concerning the upper and lower limits of normal. It is necessary, therefore, to arrive at some conclusion regarding the foregoing questions before it can be said that certain diseases do or do not cause the heart to enlarge. In this study I have attempted to learn something definite with regard to the weight of the normal heart.

MATERIAL

Ideal material for such study obviously cannot be obtained since the heart after death is not absolutely comparable to the normal heart during life. The nearest approach to ideal material would be a heart obtained from a person dying suddenly from accidental causes who had been in perfect health as revealed by recent general examination. It would, of course, be impossible to obtain enough material of this type to give any conclusive results. The most ideal available material is that of hearts obtained from patients who have died from diseases that have not affected the size or weight of this organ.

The most satisfactory material for this study was obtained from accident cases with and without operation. Other satisfactory material came from cases of acute and chronic appendicitis, hernias, and gynecological cases in which the patient had died from pulmonary embolism, pneumonia, or shock following operation. A large percentage of cases were carcinoma of the stomach, breast, colon and sigmoid, tumor of the brain, and peritonitis following operation for lesions of the gall bladder, bowel, prostate and kidneys.

The age, sex, height, weight of the body, weight of the heart, anatomical diagnosis, gross and microscopic diagnosis of the condition of the heart, the blood pressure readings, and the degree of existent arte-

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riosclerosis were obtained from necropsy records and clinical histories in The Mayo Clinic in 1000 cases.

Cases Excluded.—If specimens are to be used only from cases in which the disease did not affect the size or weight of the heart, it is apparent that a large percentage of cases examined in any gross series will be rejected.

The records of all diseases known or supposed to affect the weight of the heart were excluded. All cases of lesions of the heart were discarded, as well as those in which a clinical diagnosis had been made of cardiac disease, that is, pericarditis, endocarditis, and diseases of the myocardium, such as fatty changes, myocarditis, arteriosclerosis, hypertrophy, and dilatation. All cases of systemic diseases that are commonly believed to affect the size and weight of the heart were rejected. Among these were syphilis, pernicious anemia, arteriosclerosis exceeding Grade 1, chronic nephritis, hypertension,* exophthalmic goiter and adenomatous goiter with hyperthyroidism, and long-standing bronchial asthma. All cases presenting signs or symptoms of cardiac decompensation were excluded, as were those in which the heart was enlarged without demonstrable cause. By this method of selection, the number of acceptable cases was greatly reduced as evidenced by the fact that 6000 protocols were examined in order to obtain the 1000 used in this series.

Weight of the Body.—Practically all of the patients had been weighed during their examination at the clinic and had also stated their normal weight. If there was a marked difference between the weight at entrance and the normal weight, the latter was used. This difference was especially noteworthy in cases of malignant tumors in some of which from 20 to 40 pounds had been lost. An objection might be made to this material. If the normal weight of the body is accepted the weight of the heart will be relatively small, since it may have lost a little of its fat. If, however, the entrance weight is accepted the error would be much greater. In like manner, the normal weight given by the patient generally includes the clothing, whereas the entrance weight includes only a sheet and cape, weighing approximately 0.68 kg. (1.5 pounds). It is not likely that these slight inherent errors in technic have influenced the results appreciably.

LITERATURE

Boyd[4] (1861) studied this subject from cadavers at Morylebone Infirmary and from an insane asylum at Sommerset. He apparently did not select his material.

Thoma,[16] Müller,[12] Vierordt,[17] and Kress[10] made extensive investigations. Vierordt and Kress, however, did not record weights. Thoma's figures are based on the average weight of the heart from

*Systolic blood pressure readings exceeding 145 for any age.

published data combined with his own study of the average weight of the body for corresponding ages. Müller weighed both the heart and the body but, so far as can be determined, did not consider the clinical data. A considerable percentage of the cases in many of his studies were of extremely emaciated infants. He studied the relation of the weight of the heart, and of the muscle of the heart, to the weight of the heart as a whole and to the weight of the body, and also its relation to height and age (Table I).

From their results it is apparent that there must be a correlation between the weight of the body and that of the heart, probably due to the "need of a given mass of heart muscle to pump the blood to a given mass of tissue."

Bardeen[2] concluded that 0.55 per cent of the body weight approximated closely the normal relative proportion of the weight of the heart in males at all ages except at birth and immediately thereafter (Table I). In females, the relative proportion is about 0.53 per cent of the body weight.

From Müller's observations (Table I) the weight of the heart is approximately 0.50 to 0.75 per cent of the weight of the body in persons of normal height and weight, being slightly higher in males and lower in females; higher in thin persons and lower in obese persons. Müller concluded that there is "an increase in the relative weight of the heart with age, *irrespective of the size of the body.*"

Gray[8] has stated that the heart continues to increase in weight and size up to an advanced period of life and that this increase is more marked in men than in women.

Müller found that the weight of the left ventricle is approximately twice that of the right ventricle. The ventricles weigh approximately four times as much as the auricles, and the weight of the valves is 2 per cent of the total weight of the heart. The fat content increases with age. In the newborn infant there is relatively little fat. He found in males that the relative weight of cardiac fat to body weight is 0.077 per cent in the range from two to fifty years with 0.057 per cent as the minimum. Below the second year, he found the percentage much less, and after fifty years it is considerably greater. He also estimated that the intrapericardial part of the great vessels of the heart is 0.005 per cent of the weight of the body. This is increased with age. The weight of the heart is 5.5 gm. per kilogram of body weight and its specific gravity is about 1.050.

Greenwood and Brown[9] concluded that there is a correlation between the weight of the heart and the weight of the body, and that the weight of the heart can be calculated from the weight of the body with an error of about 8 per cent. They found that by dividing the weight of the heart by the weight of the body, the heart is approximately 0.575 per cent of the body weight. There was a variation from

TABLE I

PROPORTIONAL WEIGHT OF THE HEART AT VARIOUS AGES AS REPORTED BY SEVERAL INVESTIGATORS

AGE	OBSERVER																	
	BOYD				THOMA	MÜLLER				VIERORDT				KRESS				
	MALE		FEMALE			MALE		FEMALE		MALE		FEMALE		MALE		FEMALE		
	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	ESTIMATE BASED ON VARIOUS DATA	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY
Birth	44	0.648	42	0.572	0.625	23	0.62	14	0.63	62	0.76	59	0.80	3	0.66	6	0.89
months																	
1	16	0.594	21	0.651		45	0.64	47	0.63	7	0.51	12	0.49	2	0.83		
2-3						50	0.58	52	0.61	30	0.48	33	0.38	6	0.68	7	0.65
4-6	15	0.605	24	0.716	0.444					28	0.38	26	0.36	8	0.67	11	0.64
7-9										29	0.40	18	0.29	7	0.64	9	0.65
10-11	46	0.516	40	0.628		34	0.60	32	0.60	6	0.41	6	0.44	6	0.54	5	0.67
years																	
1					0.412					15	0.46	18	0.42	4	0.59	7	0.58
2	34	0.736	32	0.711	0.422	34	0.62	42	0.62	45	0.47	52	0.53	12	0.60	4	0.60
3	27	0.662	29	0.716	0.417					31	0.52	37	0.50	10	0.58	7	0.61
4					0.40	16	0.58	19	0.59	32	0.53	18	0.55	10	0.64	8	0.61
5					0.382					24	0.51	30	0.55	8	0.54	7	0.60
6	27	0.676	20	0.592	0.383					7	0.48	17	0.56	7	0.65	7	0.64
7					0.392					18	0.47	6	0.48	7	0.61	5	0.64
8					0.402	15	0.62	18	0.56	3	0.44	11	0.58	5	0.80		
9					0.417					6	0.46	4	0.62	5	0.65	2	0.66
10					0.433					10	0.51	3	0.54	5	0.60	2	0.58
11					0.452					12	0.52	5	0.47	2	0.49	2	0.60
12					0.474					1	0.34	1	0.40				
13	21	0.634	17	0.706	0.481	9	0.60	10	0.55	8	0.50	2	0.46	2	0.63	3	0.54
14					0.490					8	0.58	8	0.50	4	0.61	1	0.60
15					0.500					9	0.48	11	0.65	5	0.62	35	0.52

TABLE I—CONT'D

AGE	OBSERVER																	
	BOYD				THOMA	MÜLLER				VIERORDT				KRESS				
	MALE		FEMALE			MALE		FEMALE		MALE		FEMALE		MALE		FEMALE		
	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	ESTIMATE BASED ON VARIOUS DATA	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	CASES	PER CENT OF WEIGHT OF BODY	
16					0.481					11	0.51	10	0.63					
17					0.471					17	0.51	16	0.52					
18	18	0.699	15	0.762	0.474	23	0.55	13	0.50	20	0.46	25	0.49					
19					0.474					23	0.51	15	0.53					
20					0.476					15	0.51	30	0.48					
21					0.481					33	0.49	22	0.48					
22					0.483					27	0.50	21	0.48					
23					0.490					24	0.48	22	0.49					
24					0.495					30	0.46	22	0.49					
25-30	58	0.675	74	0.654	0.502	73	0.58	45	0.50	30	0.46	27	0.49					
	46	0.597	29	0.608														
31-40	118	0.720	87	0.682		70	0.56	59	0.52									
	59	0.600	49	0.470														
41-50	137	0.705	106	0.706		84	0.59	69	0.56									
	76	0.690	49	0.676														
51-60	119	0.719	106	0.764		87	0.62	61	0.59									
	42	0.637	39	0.710														
61-70	126	0.763	149	0.758		88	0.64	83	0.64									
	39	0.728	41	0.716														
71-80	100	0.774	150	0.786		64	0.64	61	0.67									
	21	0.693	20	0.612														
81-90	24	0.840	76	0.806		11	0.75	12	0.69									
	7	0.740	5	0.655														

the mean percentage of about 25 per cent in each direction, that is, from 0.45 per cent to 0.7 per cent of the weight of the body.

Boyd's figures show a higher percentage than do the others', ranging from 0.6 to 0.8 per cent instead of less than 0.6 per cent. He found very little differences between the percentages of males and females.

Scammon[15] concluded: "The heart weighs at birth from 20 to 25 gm. The weight of the heart at birth doubles in the first two years of life. The weight of the heart at birth triples in four years. The weight of the heart at birth increases sixfold at puberty. There is a rapid increase in heart weight during adolescence. The adult heart weighs ten to thirteen times that of the newborn. The relative heart weight of the newborn is distinctly greater than that of the adult. At birth the heart forms 0.65 to 0.80 per cent of the body weight. During the second year the relative heart weight is about 0.5 per cent of the body weight and this relation obtains, with individual variation, through the remainder of childhood and maturity."

METHOD OF STUDY AND FINDINGS

The heart consists of (1) muscles; (2) connective tissue of the valves and supporting structures; (3) intrinsic blood vessels of the heart and the great vessels near their attachments to the heart, and (4) fat beneath the pericardium and elsewhere in the heart. The length and size of large vessels left attached to the heart will affect the weight to some degree. In my study the hearts were opened and washed before being weighed. The specimens were divided according to age and then subdivided according to sex (Table II).

Accurate conclusions cannot be drawn from the age groups from five to seven years and from eighteen to twenty-one years, since there were only fourteen and twenty-nine cases respectively in these groups. In fact, all the results in the age groups up to twenty-one years are not wholly reliable or accurate because they are affected by the growth curves. The age group from forty-one to fifty years was the only group in which the percentage of body weight was higher in the females than in the males.

The highest percentages of body weight occurred in the group of premature births, 0.98 per cent for males and 0.91 per cent for females. In the group from birth to one year the percentages were 0.62 per cent for males and 0.55 per cent for females. The percentage in the remaining males ranged from 0.35 to 0.46 per cent. The adult male age groups showed a range in percentage from 0.42 to 0.46. In the female groups of all ages the percentage ranged from 0.37 to 0.91. The percentage ranged from 0.38 to 0.46 for the adult females.

TABLE II

AGE, YEARS	TOTAL NUMBER OF CASES	MALE	FEMALE	HEART WEIGHT GM.			BODY WEIGHT						HEIGHT CM.			PERCENTAGE OF BODY WEIGHT
							MINIMUM		MAXIMUM		AVERAGE					
				MINIMUM	MAXIMUM	AVERAGE	POUNDS	KILOGRAMS	POUNDS	KILOGRAMS	POUNDS	KILOGRAMS	MINIMUM	MAXIMUM	AVERAGE	
Premature	28	15		4	86	20.4	2	0.9	12	5.4	4.6	2.0	33	62	43.4	0.98
			13	8	51	22.0	3	1.3	9	4.0	5.3	2.4	32	50	45.0	0.91
Birth to 1 year inclusive	34	17		15	95	45.0	6	2.7	35	15.0	16.0	7.2	44	98	66.0	0.62
			17	10	83	35.0	4	1.8	30	13.0	14.0	6.3	42	86	63.0	0.55
2-4	27	17		45	98	69.0	16	7.2	60	27.0	35.0	15.9	44	107	86.5	0.43
			10	27	83	55.5	20	9.0	50	22.0	33.0	15.0	78	96	88.0	0.37
5-7	14	8		60	113	87.7	40	18.0	65	29.0	56.0	25.0	107	119	112.5	0.35
			6	60	144	94.0	33	15.0	90	40.0	56.0	25.0	109	131	117.0	0.37
8-12	17	13		81	186	149.0	40	18.0	110	50.0	73.5	33.0	105	153	135.0	0.44
			4	93	150	120.0	50	22.0	80	36.0	63.0	24.0	120	146	132.0	0.419
13-17	26	18		151	320	225.0	80	36.0	150	68.0	115.0	52.0	144	177	161.0	0.43
			8	120	243	180.0	50	22.0	150	68.0	103.0	46.0	151	171	160.0	0.38
18-21	29	19		225	354	308.0	110	50.0	170	77.0	149.0	67.0	159	189	174.0	0.42
			10	202	284	245.0	100	45.0	175	79.0	127.0	57.0	155	165	160.0	0.42
22-30	90	56		155	388	282.0	100	45.0	180	81.0	138.0	62.0	160	185	171.0	0.44
			34	155	310	223.0	85	38.0	195	88.0	126.0	57.0	130	172	158.0	0.38
31-40	179	98		190	380	290.0	90	40.0	190	86.0	146.0	66.0	144	195	173.0	0.44
			81	110	365	243.0	90	40.0	200	90.0	134.0	60.0	152	176	163.0	0.40
41-50	221	138		196	400	302.0	100	45.0	208	94.0	153.0	69.0	154	186	165.0	0.43
			83	148	350	270.0	95	43.0	210	95.0	127.0	57.0	145	186	162.0	0.46
51-60	222	134		140	397	294.0	110	50.0	250	113.0	148.0	67.0	159	187	171.0	0.44
			88	160	367	263.0	80	36.0	220	100.0	143.0	65.0	130	181	162.0	0.40
61-70	100	76		210	386	289.0	100	45.0	200	90.0	138.0	62.0	162	182	171.0	0.46
			24	171	305	259.0	100	45.0	221	100.0	134.0	60.0	146	172	162.0	0.42
71-80	13	13		137	375	292.0	120	54.0	170	76.0	141.0	64.0	166	185	174.0	0.45

One is impressed by the close ratios of each group. The total average of the weight of the heart of all the adult male groups is 0.43 per cent of the weight of the body and of the female is 0.40 per cent. It is possible that the percentages are slightly too high since the body weights were apparently slightly below normal (Table I).

Boyd's percentages ranged from 0.59 to 0.84 for males and 0.51 to 0.80 for females.

Thoma's average percentage of the weight of the heart varied from 0.38 to 0.49.

Müller's percentages had a scope of 0.55 to 0.75 for males and 0.50 to 0.69 for females.

Gray stated the relative weight of the heart for males as 1:160 or 0.62 per cent, and as 1:150 or 0.66 per cent for females (Table III).

Piersol found the relative weight of the heart for males to be as 1:169 or 0.59 per cent and for females as 1:162 or 0.61 per cent.

Gray and Piersol both give a relatively higher weight of the heart for the females. In only two of the age groups of my series did a relatively higher percentage weight for the females occur. In nine age groups the percentage of the male was higher and in one group the percentage for the males and females was the same.

Müller stated further: "There is an increase in the relative weight of the heart with age, irrespective of the size of the body." Gray stated: "The heart continues to increase in weight and size up to an advanced period of life" and, "This increase is more marked in males than in females." He then paradoxically stated that the weight of the heart of the female is relatively higher. Other investigators agree with Gray and Müller that the weight of the heart increases with age.

During the War, Aschoff studied the weight of the hearts of 685 soldiers (Table IV); the average weight was 321 gm.

Cruveilhier found the average weight of the heart for males to be 240 gm. and for females 210 gm.

The conclusions drawn from my study do not agree with the statement: "The weight of the heart increases with age, irrespective of weight." Probably the reason that other observers obtained a higher percentage of weight of the heart and concluded that the heart increased with age irrespective of the weight of the body was owing to the fact that they did not exclude hypertensive hearts.

The total average for all adult age groups was 294 gm. for males and 250 gm. for females. The smallest heart for the males in the adult age groups was 155 gm. and the largest was 400 gm. Only one heart weighed 400 gm. There was nothing in the history of the case to justify its exclusion. The subject was an unusually well-developed man weighing 93.6 kg. (208 pounds). The smallest heart of a female in the adult age group was 110 gm., the largest was 367 gm.

TABLE III

RELATIVE WEIGHT OF THE HEART BY VARIOUS AUTHORS

AUTHOR	AVERAGE WEIGHT OF HEART, GM.		PER CENT OF WEIGHT OF BODY	
	MALE	FEMALE		
Gray	280-340	230-280		
Davis	280	250		
Morris	321	230-250	1:205	
Piersol	266-346	230-340	Male 1:169 or 0.59	Female 1:162 or 0.61
Cunningham	310	255	Birth 1:139 0.76	Adult 1:205 0.5+

TABLE IV

WEIGHT OF HEART AMONG SOLDIERS (ASCHOFF)

AGE, YEARS	HEIGHT, METERS	WEIGHT OF HEART, GM.
18-19	1.65	300 (19)*
20-24	1.70	299 (133)
25-29	1.72	327 (102)
30-34	1.72	328 (85)
35-39	1.75	319 (65)
40-44	1.69	355 (45)
45-50	1.66	319 (19)

*Number in parenthesis denotes number of 468 cases in each group.

The smallest weight of the body in the adult male group was 40.5 kg. (90 pounds) and the largest was 112.5 kg. (250 pounds). The average was 64.8 kg. (144 pounds). The smallest weight of the body in the adult female group was 38.3 kg. (85 pounds) and the largest 99.5 kg. (221 pounds). The average was 59 kg. (131 pounds). There were relatively few of the extremely small or large weights.

In this series the weight of the heart did not increase with age. The largest male hearts were in the age groups eighteen to twenty-one years, but in each group the weight was quite constant. The average weight of the heart varied from 282 to 308 gm. In the last group there were only thirteen cases, but these thirteen cases conformed with the other age groups. In Fig. 1 where the weight of the heart over weight of the body is plotted against the age groups, there is a sudden fall followed by virtually a straight line. Only twice does the female line cross the male and that is in the five to seven year and in the forty-one to fifty year age groups. In Fig. 2 the weight of the heart is used as the ordinate and the age group as abscissa. The curve from birth up to the adult period simulates Scammon's growth curve and from the beginning of the adult period on tends to follow a straight line. In Fig. 3 the heart weight in grams is plotted against the body height in centimeters. One can reasonably conclude from this curve that the height affects the heart weight only as the height affects the body weight.

In 1914 Allen Hazen ruled some paper with a horizontal scale, so divided that the curve of probability would plot a straight line and hence any series of observations which varied in accordance with the law of arithmetic probability would also plot as straight lines. The

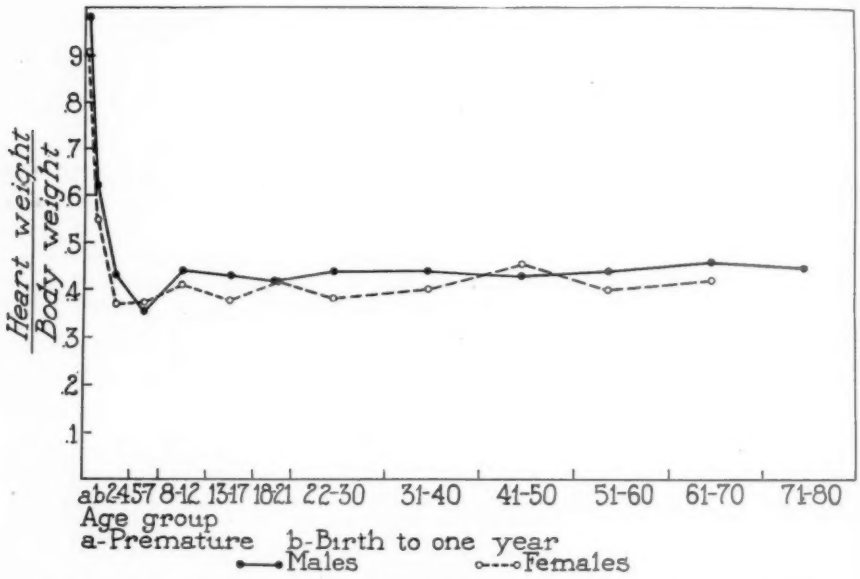

Fig. 1.—Ratio of weight of heart to weight of body for various age groups.

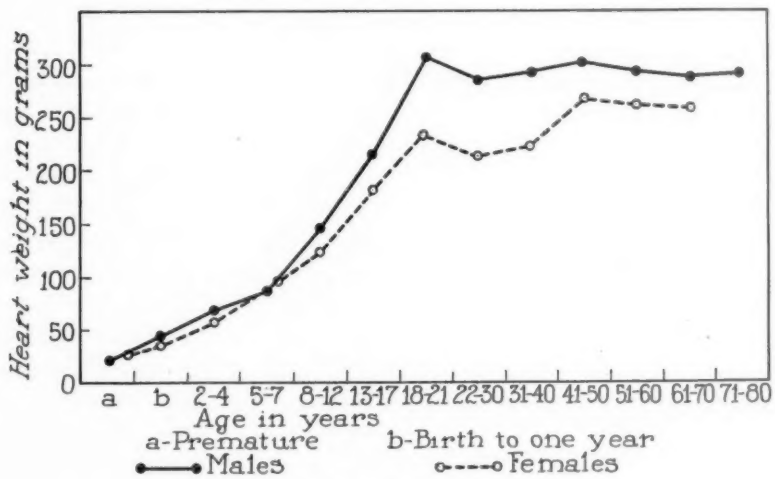

Fig. 2.—Weight of heart for various age groups.

converse is also true, that is, any series of observations plotted on this paper that plot a straight line will vary in accordance with the law of arithmetic probability.

The different age groups were taken, male and female, and plotted on probability paper and all plotted fairly straight lines (Figs. 4 and

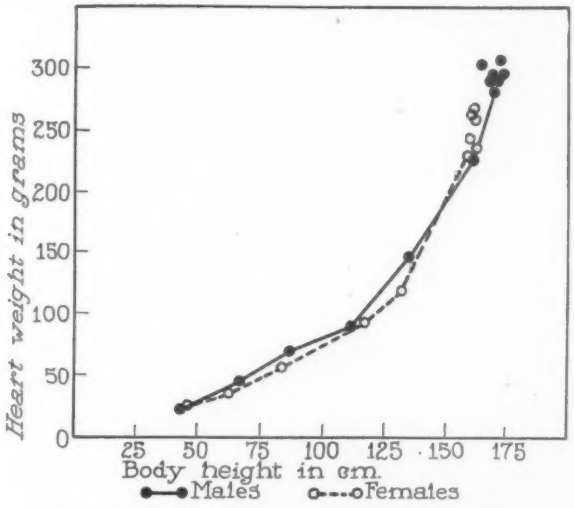

Fig. 3.—Relation of weight of heart to height.

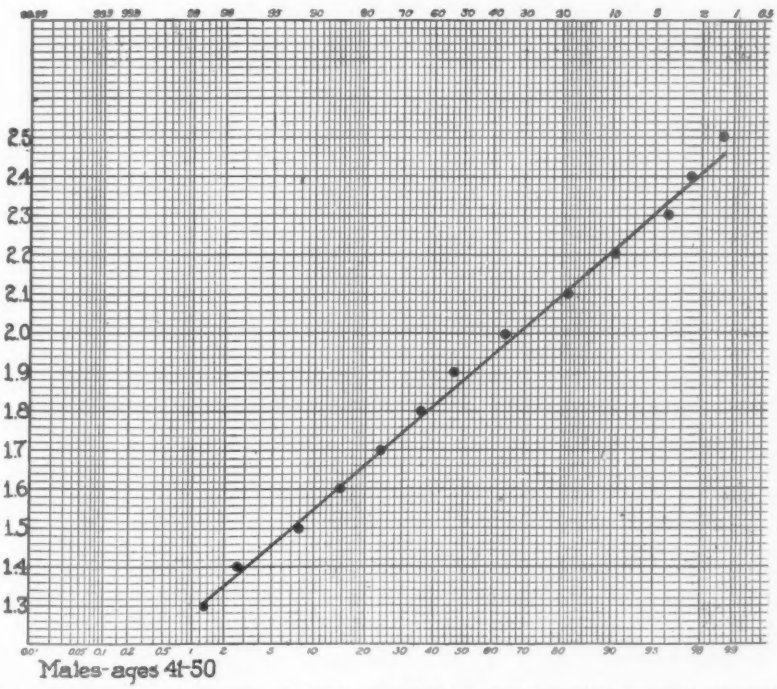

Fig. 4.—Percentage of weight of heart to weight of body plotted against percentage of cases for males aged from forty-one to fifty.

5). For the abscissas the percentage of the number of cases was used and the percentages of heart weights to body weights as the

ordinates. In Fig. 4 (males aged from forty-one to fifty) there were 1.2 per cent of that group in which the ratio of the weight of the heart to the weight of the body was 1.3 or less. There were 2.3 per cent in which the ratio was 1.4 or less and 10 per cent in which the ratio was 1.5 or less. In 15 per cent the ratio was 1.6 or less, in 25 per cent 1.7 or less, in 37 per cent 1.8 or less, in 48 per cent 1.9 or less, in 66 per cent 2.0 or less, in 82 per cent 2.1 or less, in 91 per cent 2.2 or less, in 97 per cent 2.3 or less, in 98.5 per cent 2.4 or less, and in 99.5 per cent 2.5 or less.

Fig. 6 represents the curves with low and high weights of the body. The curve for low weights is more vertical than the one for

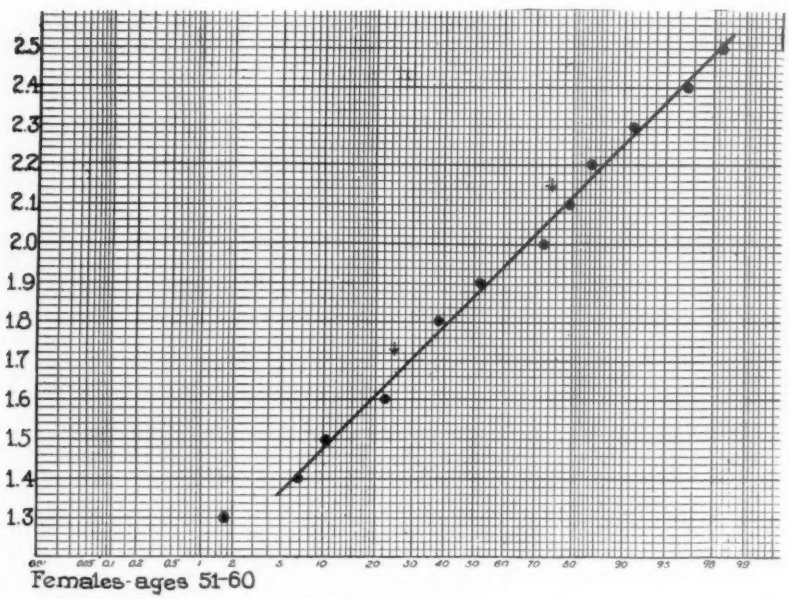

Fig. 5.—Percentage of weight of heart to weight of body plotted against percentage of cases for females aged from fifty-one to sixty.

high weights. The average ratio for the high weights is lower than that for the average weights. The average ratio for low weights is 1.9 and for the high it is 1.6.

Variation.—When many different measurements of a certain quantity have been made, it is common to generalize them by computing the averages, that is, the numerical mean. This often fails to give a complete visualization of the individual measurements in a series. Two groups of items of very different magnitude may yield the same average; for example, the average of 5, 6, 5, 8 and 6 is 6, and likewise the average for 1, 2, 1, 3 and 23 is 6.

In my series of cases relatively few very low or very high weights

of the body occurred. Among 532 adult males there were twenty-four exceeding 86 kg. (190 pounds) and thirty-three below 54 kg. (120 pounds).

In Table V the weight of the heart in normal males was obtained by multiplying the weight of the body by the ratio which was found to be 1.96 for the average, 1.5 for the minimum and 2.3 for the maximum. This ratio holds true for the average weight of the body, but in the higher weights, the ratio is lower. In Fig. 6 are plotted all the higher weights and the ratio was found to be as low as 1.6. It is therefore difficult to construct a table and include all the weights of the body both the extremely low and the extremely high. If the

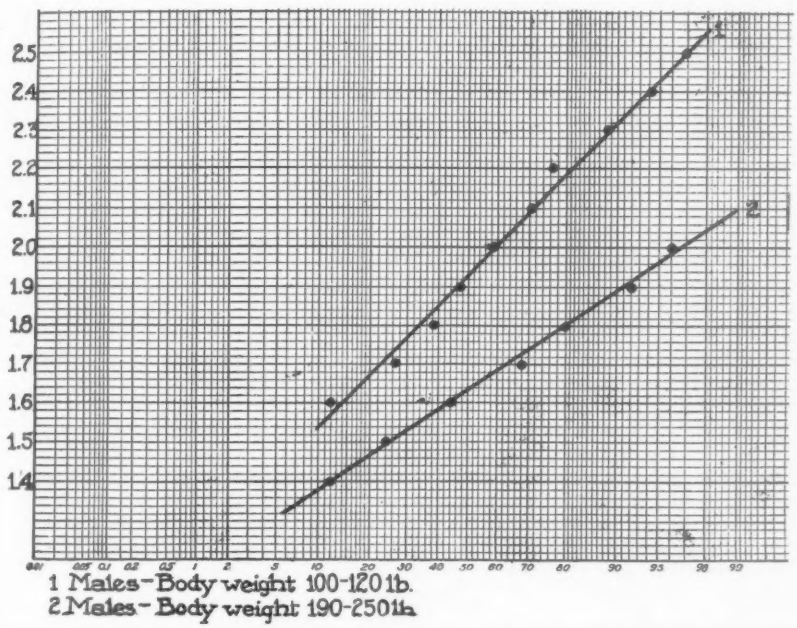

Fig. 6.—Percentage of weight of heart to weight of body plotted against percentage of cases; 1, males of low weight; 2, males of high weight.

ratio 4.3 for a body weight of 86 kg. (190 pounds) is used, there will result a higher heart weight than will occur in an individual weighing 103.5 kg. (230 pounds), if the ratio 1.6 is employed.

To obtain the weight of the male heart, the weight of the body in kilograms may be multiplied by 4.3. This will give the heart weight in grams. Example: Body weight 68 kilograms times 4.3 = 292 gm.

In Table VI of normal weights of the female heart, the average weight is obtained by multiplying the weight of the body by the ratio 1.8.

The maximal weight of the heart is obtained by using the ratio 2.15, and the minimal weight of the heart by using the ratio 1.5.

TABLE V

NORMAL WEIGHT OF THE HEART: MALES

BODY WEIGHT		MINIMUM	AVERAGE	MAXIMUM
POUNDS	KILOGRAMS	GM.	GM.	GM.
105	47	165	205	241
110	50	173	215	253
115	52	181	225	264
120	54	190	235	276
125	56	198	245	287
130	58	206	255	299
135	60	213	265	310
140	63	221	274	322
145	65	229	284	333
150	68	237	294	345
155	70	245	304	356
160	72	253	313	368
165	74	261	323	370
170	77	268	333	371
175	79	280	343	372
180	81	288	353	373
185	83	296	363	382
190	86	304	373	392
195	88	312	382	402
200	90	320	392	412

TABLE VI

NORMAL WEIGHT OF THE HEART: FEMALES

BODY WEIGHT		MINIMUM	AVERAGE	MAXIMUM
POUNDS	KILOGRAMS	GM.	GM.	GM.
90	40	135	162	193
95	43	143	171	204
100	45	150	180	215
105	47	158	189	226
110	50	165	198	237
115	52	172	207	248
120	54	180	215	259
125	56	188	225	268
130	58	195	234	277
135	60	203	244	286
140	63	211	253	295
145	65	219	262	304
150	68	225	272	313
155	70	233	282	322
160	72	240	288	330
165	74	247	297	337
170	77	255	306	343
175	79	283	315	350
180	81	301	324	356
185	83	309	333	361
190	86	317	342	366
195	88	325	351	371

CONCLUSIONS

1. The average weight of the adult male heart is 294 gm.; the average weight of the adult female heart is 250 gm.

2. There is a definite correlation between weight of the heart and weight of the body. The ratio is 0.43 per cent for males, and 0.40

per cent for females. The ratio is slightly higher in thin persons and lower in obese persons. This coefficient is not so accurate for body weights of less than 45 kg. (100 pounds) and more than 94.5 kg. (210 pounds).

3. The weight of the heart may be calculated from the weight of the body with an error varying from 8 to 10 per cent.

4. The weight of the heart does not increase with age, irrespective of the weight of the body. The weight of the heart increases with increase in weight of the body.

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OBSERVATIONS ON THE MORTALITY OF HEART DISEASE IN NEW YORK STATE*

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THESE remarks are based upon information gathered by and for the Committee to Study Heart Disease of the New York State Medical Society.†

The importance of the mortality of heart disease in the State mortality statistics is shown by the comparison of its yearly rate per 100,000 with six other principal causes of death. The term heart disease includes the four numbers of the International List. In the graphic comparison (Fig. 1) there are two striking features: first, the curve of rates for heart disease is well above all the other rate curves and, second, since 1917 (Table I) the rate has risen progressively from 251 to 303 in 1926. Compared with the tuberculosis curve, it is evident that they are diverging persistently. The rate curve of cancer is observed to be rising but not so rapidly as the curve of heart disease.

In the United States Registration Area in 1925 the heart disease mortality rate per 100,000 was only 186, but this curve, too, was above all others, though not so much above as was the curve in New York State. The death rate for tuberculosis is fifth in importance in the United States Registration Area, but is seventh in the State, including accidents. Heart disease accounts in New York State for 21 per cent of all deaths, but in the United States Registration Area for only 15 per cent of deaths.

TABLE I

DEATH RATES PER 100,000 FROM SEVEN PRINCIPAL CAUSES OF DEATH

New York State Exclusive of New York City
1917-1926

CAUSE OF DEATH	1926	1925	1924	1923	1922	1921	1920	1919	1918	1917
Diseases of the Heart	303	273	261	270	260	234	243	221	247	251
Cerebral Hemorrhage	126	120	131	128	132	128	127	123	126	127
Cancer	121	121	120	117	115	114	109	106	104	103
Nephritis	121	118	112	111	111	110	117	116	128	136
Pneumonia	117	98	92	115	109	85	138	129	293	161
Accidents	86	89	88	90	82	76	78	76	88	97
Tuberculosis	85	89	91	95	95	99	112	126	145	138

*Read at the Fifth Annual Scientific Session of the American Heart Association, in Minneapolis, June, 1928.

†The detailed report of this study has been published in pamphlet form by the Medical Society of the State of New York.

If now the deaths for six leading causes of death are plotted (Tables II-A and B, and Fig. 2) by small age groups, the order of importance appears to be heart disease, cancer, cerebral hemorrhage, nephritis, pneumonia, and tuberculosis. Another interesting fact is that the number of deaths (Table II) from heart disease (14,480) is greater than the total number of deaths from both cancer (6,417) and tuber-

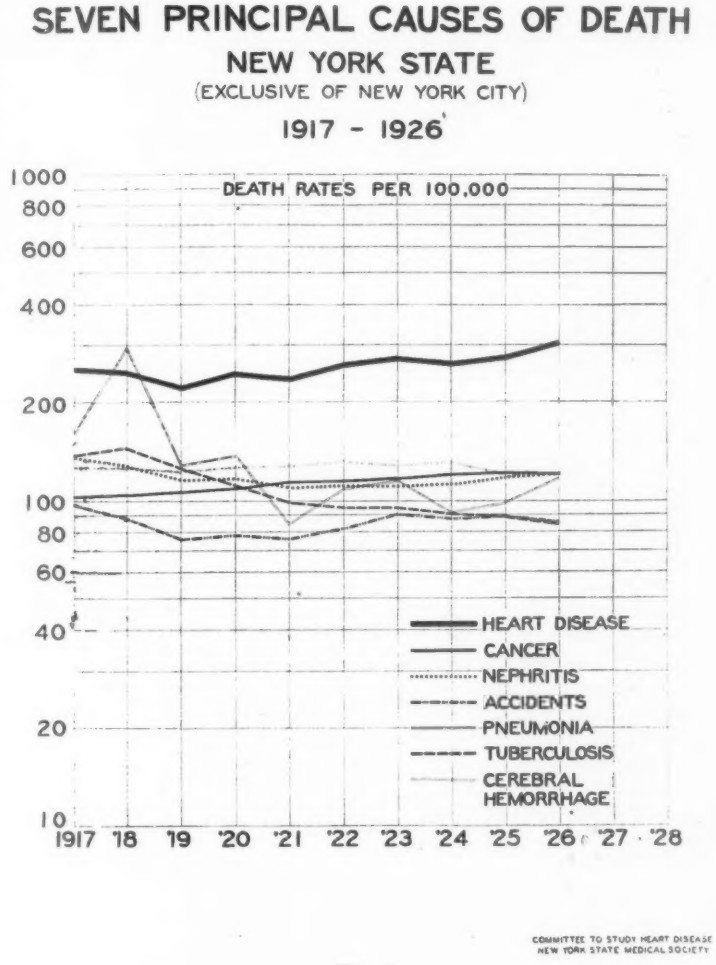

Fig. 1

culosis (4,698). In the United States Registration Area deaths from heart disease do not equal the sum of the deaths from cancer and tuberculosis.

The greatest number of deaths from heart disease, cerebral hemorrhage, and pneumonia occurs in the age group seventy to seventy-four years, while the greatest number of deaths from cancer and nephritis

TABLE II-A

DEATHS FROM SIX LEADING CAUSES BY AGE GROUPS

New York State Exclusive of New York City
1915

AGE GROUPS	DISEASES OF THE HEART	CANCER	CEREBRAL HEMORRHAGE	NEPHRITIS	PNEUMONIA	TUBERCULOSIS
All Ages	14,480	6,41[illegible]	6,332	6,259	5,174	4,698
Under 5	116	14	25	37	1,298	215
5-9	89	7	4	19	87	63
10-14	126	8	7	19	66	62
15-19	121	8	5	40	81	345
20-24	114	24	10	43	102	559
25-29	135	43	13	46	116	621
30-34	163	80	24	105	149	596
35-39	269	157	46	159	200	464
40-44	422	296	105	230	258	373
45-49	583	439	184	322	257	326
50-54	826	613	346	414	275	277
55-59	1,059	804	469	549	261	203
60-64	1,481	873	721	676	343	213
65-69	1,904	948	940	886	403	170
70-74	2,103	875	1,134	865	411	112
75-79	2,078	663	1,029	821	338	60
80-84	1,624	376	758	617	295	29
85-89	888	139	358	282	153	5
90 and Over	371	47	152	123	78	1
Unknown	8	3	2	6	3	4

TABLE II-B

DEATHS FROM SIX LEADING CAUSES BY AGE GROUPS

New York State Exclusive of New York City
1915

AGE GROUPS	DISEASES OF THE HEART	CANCER	CEREBRAL HEMORRHAGE	NEPHRITIS	PNEUMONIA	TUBERCULOSIS
All Ages	10,820	4,649	5,440	6,068	6,288	6,195
Under 5	130	9	28	115	1,928	398
5- 9	72	11	4	26	90	99
10-14	90	7	1	20	49	116
15-19	87	9	4	41	70	422
20-24	98	19	9	87	118	748
25-29	147	36	17	111	126	758
30-34	177	83	29	135	134	690
35-39	234	145	62	203	179	644
40-44	313	253	106	250	239	552
45-49	437	381	190	366	255	456
50-54	614	517	306	467	278	395
55-59	826	584	503	544	317	292
60-64	1,085	601	609	680	407	235
65-69	1,382	668	733	794	432	157
70-74	1,697	541	908	783	513	117
75-79	1,529	428	905	699	479	68
80-84	1,120	239	608	484	376	37
85-89	572	81	309	200	194	10
90 and Over	210	36	109	60	104	1
Unknown	---	1	---	3	---	---

occurs in the age group sixty-five to sixty-nine years. The number of deaths from tuberculosis has diminished and the highest point of the curve is in the age group twenty-five to twenty-nine years, after which the curve falls persistently. The deaths from tuberculosis considerably exceed those from heart disease until the age of forty, after which time the deaths from heart disease far exceed those from tuberculosis.

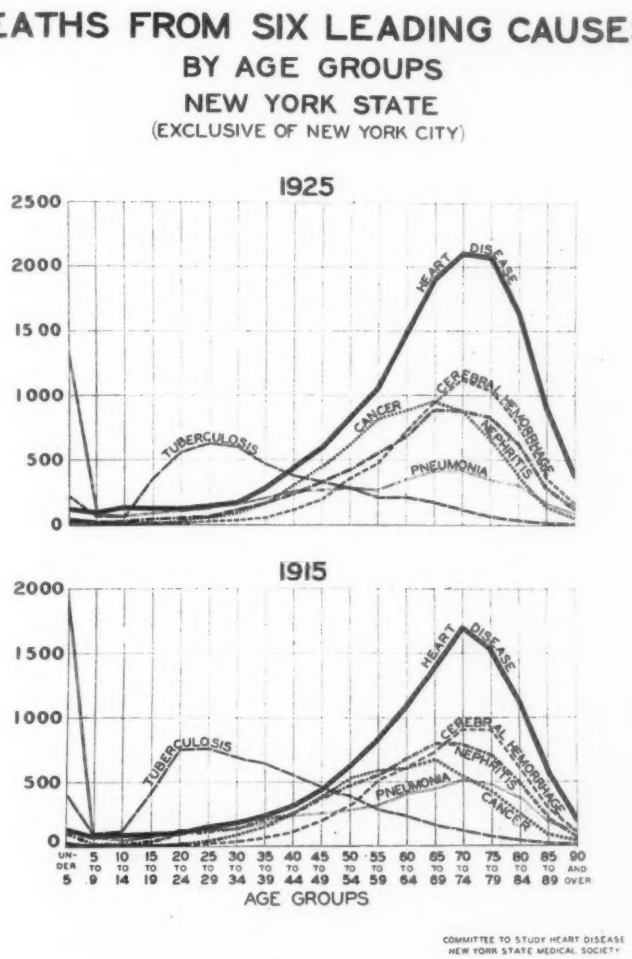

Fig. 2.

If now the comparison is made by cumulative percentage (Table III and Fig. 3) of the population, all deaths, and deaths from heart disease, by small age groups, certain interesting facts become apparent.

First, 50 per cent of the population is under the age of thirty years, while 50 per cent of the deaths from all causes occur under the age of sixty. The curve of heart disease deaths for 1925 has moved toward

TABLE III

CUMULATIVE DISTRIBUTION BY AGE GROUPS OF HEART DISEASE DEATHS FOR 1915 AND 1925

With All Deaths and Population for 1925

New York State Exclusive of New York City

AGE	HEART DISEASE DEATHS				ALL DEATHS		POPULATION	
	1925		1915					
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Under 5	116	0.8	130	1.2	9,361	13.3	510,312	9.6
" 10	205	1.4	202	1.9	10,410	14.7	1,013,528	19.2
" 15	331	2.3	292	2.7	11,217	15.9	1,471,466	27.8
" 20	452	3.1	379	3.5	12,439	17.6	1,844,226	34.9
" 25	566	3.9	477	4.4	14,077	19.9	2,229,356	42.1
" 30	701	4.8	624	5.8	15,871	22.5	2,656,823	50.2
" 35	864	6.0	801	7.4	17,951	25.4	3,077,047	58.2
" 40	1,133	7.8	1,035	9.6	20,398	28.9	3,485,300	65.9
" 45	1,555	10.7	1,348	12.5	23,279	33.0	3,842,077	72.6
" 50	2,138	14.8	1,785	16.5	26,680	37.8	4,182 673	79.1
" 55	2,964	20.5	2,399	22.2	30,722	43.5	4,484,165	84.7
" 60	4,023	27.8	3,225	29.8	35,486	50.2	4,727,678	89.3
" 65	5,504	38.0	4,310	39.8	41,326	58.5	4,935,467	93.3
" 70	7,408	51.2	5,692	52.6	48,132	68.1	5,080,693	96.0
" 75	9 511	65.7	7,389	68.3	55,188	78.1	5,179,213	97.9
" 80	11,589	80.1	8,918	82.4	61,623	87.2		
" 85	13,213	91.3	10,038	92.8	66,688	94.4		
" 90	14,101	97.4	10,610	98.1	69,407	98.3		
All Ages	14,472	100.0	10,820	100.0	70,642	100.0	5,291,323	100.0
Unknown	8						4,337	

TABLE IV

PERCENTAGE DISTRIBUTION OF TYPES OF HEART DISEASE BY AGE GROUPS

For New York State Exclusive of New York City
1925

AGE GROUP	ALL FORMS	FORMS OF HEART DISEASE			
		PERICARDITIS	ENDOCARDITIS AND MYOCARDITIS	ANGINA PECTORIS	OTHER FORMS
All Ages	14,480	0.3	3.8	7.4	88.5
Under 5	116	1.7	35.4	0.0	62.9
5-14	215	1.4	31.6	0.0	67.0
15-24	235	0.4	31.1	0.4	68.1
25-44	989	0.5	17.5	5.9	76.1
45-64	3,949	0.2	2.6	11.0	86.2
65 and Over	8,968	0.3	1.1	6.4	92.2
Unknown	8				

the right, or older age side of the chart. Fifty per cent of the deaths from heart disease have not occurred until the age of seventy—ten years later than half the deaths from all causes. It is noteworthy that only 10 per cent of the deaths from heart disease have occurred at the age of forty-five years.

Ninety per cent of the deaths from heart disease occur after the age of forty-five. Heart disease then appears to be a disease of advanced

and old age, and it suggests that the prolongation of life may be a factor in the increasing number of deaths ascribed to cardiac disease.

The grouping of the types of heart disease by percentage distribution (Table IV and Fig. 4) shows 88.5 per cent of all the deaths to fall in "Other Forms" (No. 90) of the International List. Only 3.8 per cent of deaths fall in the group endocarditis and myocarditis (acute); with 35.4 per cent occurring under five years and 31 per cent

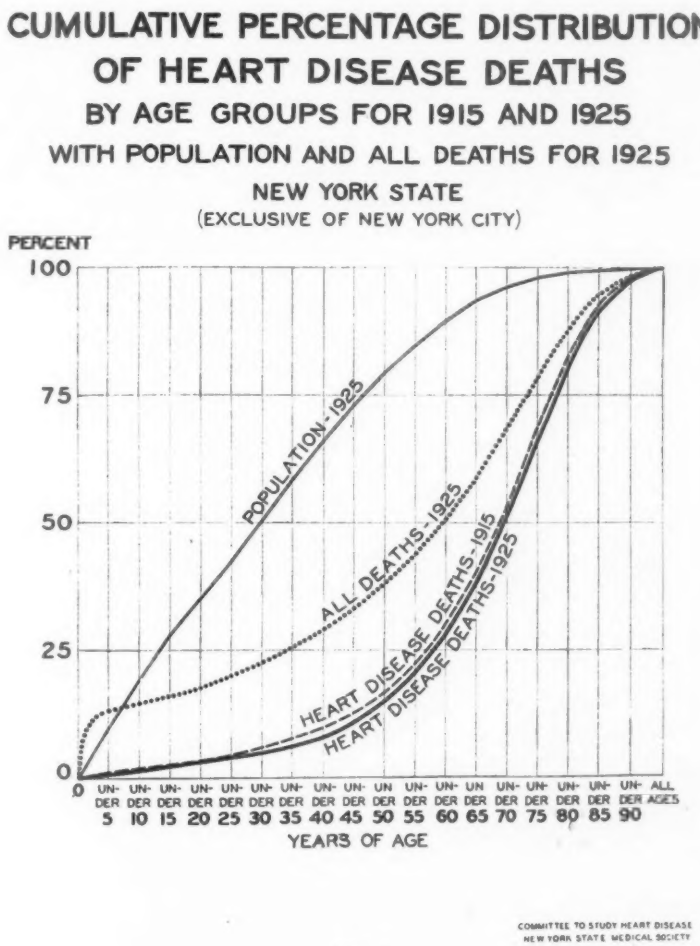

Fig. 3.

each in the age groups of five to fourteen and fifteen to twenty-four. These percentage distributions are what one meets in practice but the numerical insignificance of the whole group is astonishing, particularly in view of the very scanty analysis of the group "Other Forms" which comprises over 88 per cent of all the deaths from heart disease.

"Other Forms" is officially divided into five headings: chronic

valvular disease, aortic insufficiency, chronic endocarditis, chronic myocarditis, and fatty degeneration; but selecting the diagnoses under which most of the certificates group themselves, it appears that there are really ten headings (Table V), which differ, however, from those of the official list. These ten were studied.

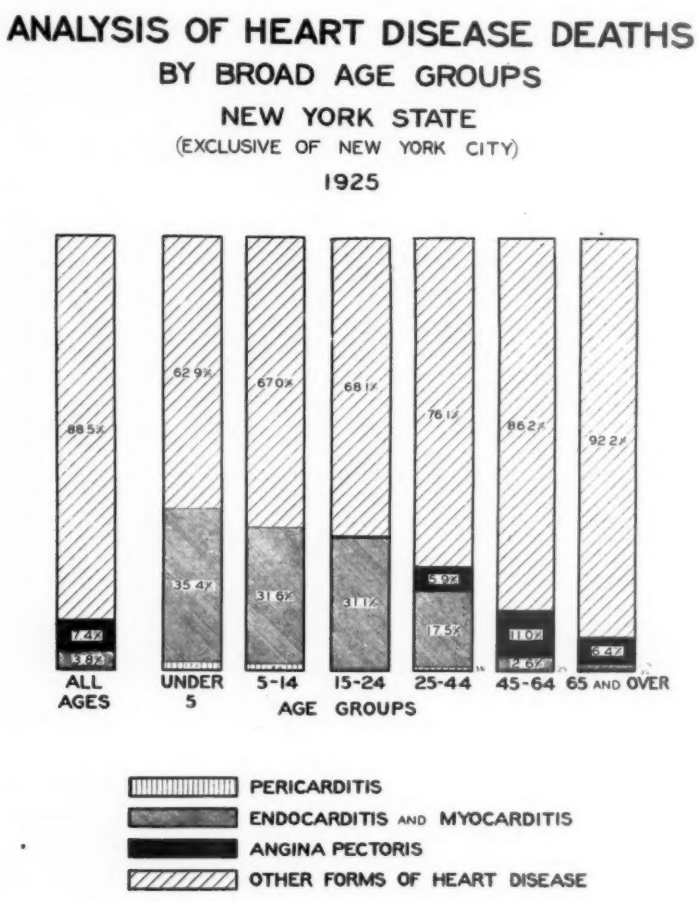

Fig. 4.

The striking fact is evident at once that the column "Chronic Myocarditis" includes nearly half of all the diagnoses in 1926, while in 1922 it accounted for only slightly over one-third (34.1 per cent). The column "Valvular Disease," which in 1922 contained nearly one quarter (23 per cent), now has only slightly over 15 per cent (15.7). The other subgroups show in 1926 only a slight decrease from the figures of 1922. It seems justifiable, therefore, to infer that there has been a trend in the fashion of diagnosis from the valvular lesions

TABLE V

OTHER DISEASES OF THE HEART. NUMBER OF DEATHS BY BROAD AGE GROUPS AND PERCENTAGE OF DEATHS FROM EACH TYPE

New York State Exclusive of New York City
1926

AGE GROUPS	TOTAL DEATHS	PERCENTAGE									
		CHRONIC MYOCARDITIS	CHRONIC ENDOCARDITIS	VALVULAR DISEASE OF THE HEART	MITRAL REGURGITATION	MITRAL STENOSIS	CARDIAC INSUFFICIENCY	DISEASES OF THE AORTA	CARDIAC HYPERTROPHY AND DILATION	CARDIORENAL DISEASES	OTHER DISEASES OF THE HEART
All Ages	14,862	48.6	12.4	15.7	3.6	1.4	4.8	2.1	3.4	0.7	7.8
Under 5	75	4.0	6.7	32.0	5.3	4.0	18.7	4.0	13.3	–	12.0
5 to 14	117	7.7	33.3	32.5	9.4	5.1	5.1	0.9	3.4	–	2.6
15 to 24	183	12.0	27.3	28.4	2.7	4.4	8.2	2.2	4.9	–	9.9
25 to 44	717	28.7	19.5	19.0	4.5	4.9	6.6	3.3	5.6	0.8	7.1
45 to 64	3,717	46.2	13.9	15.4	3.0	1.6	4.4	2.4	5.0	0.7	7.4
65 and Over	10,049	52.4	10.9	15.0	2.9	0.9	4.6	1.9	2.6	0.7	8.1
1922											
All Ages	11,509	34.1	13.0	23.0	4.4	1.3	5.1	2.5	4.8	1.3	10.5
Under 5	109	2.7	5.5	40.4	3.7	0.9	16.5	1.8	12.8	–	15.6
5 to 14	125	3.2	27.2	33.6	10.4	4.8	12.8	1.6	3.2	–	3.2
15 to 24	157	9.6	28.0	18.5	9.5	5.1	8.3	4.5	8.9	0.6	7.0
25 to 44	651	14.7	17.1	29.0	5.1	4.8	6.6	3.2	9.8	0.6	9.1
45 to 64	2,777	29.9	12.9	24.3	4.5	1.3	4.5	3.2	6.4	1.5	11.5
65 and Over	7,686	38.8	12.2	21.8	4.1	0.8	4.8	2.2	3.7	1.3	10.3

to the lesions of the heart muscle. There has been dissatisfaction with the consideration of valvular lesions as a cause of death and chronic inflammation of the heart muscle has been preferred as an explanation. This preference accounts for the fact that a very large percentage of the deaths in the age groups after twenty-five fall within the column "Chronic Myocarditis." Pathologists tell us that chronic myocarditis is one of the relatively rare conditions to be found in the heart, fibrosis of the myocardium being much the more common finding; yet this latter diagnosis has not been used in death certificates frequently enough to form a group for consideration.

The review of the death certificates gathered from the four numbers of the International List reveals the fact that there is no statement whatever concerning the etiological factor of the diseased heart. Only the most common anatomical deformities, which may well be due to several causative agents, are named. It would seem, therefore, that before a logical statement as to the accurate number of deaths due to heart disease can be made, some way must be devised to tabulate the damage under etiological headings, such as those of rheumatic fever, syphilis, other bacterial infections, and senescence or arteriosclerosis. To accomplish this physicians must accept and use recognized crite-

ria for diagnosis which include three factors—those of etiology (active or inactive), of anatomical or structural defect, and of pathological physiology.

The statistician must then tabulate the various anatomical defects according to etiology, instead of, as at present, listing such anatomical defects as causative conditions.

In other words, if we are to learn anything about the causes of death from heart disease, we, as physicians, must make diagnoses which give the etiology of the heart damage; the statistician, responsible for the records of Boards of Health Bureaus of Statistics, must arrange his machinery to tabulate the facts.

(*For discussion, see page* 116.)

HEART FAILURE AND HYPERTHYROIDISM*

With Special Reference to Etiology

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FIVE hundred cases of hyperthyroidism personally examined during the past fifteen months at the Lahey Clinic have been reviewed for the purpose of answering the following questions which pertain to the etiology of heart failure in thyrotoxicosis.

First—Does thyrotoxicosis injure the healthy normal heart muscle or is a previously damaged heart necessary for the production of congestive heart failure in hyperthyroidism?

Second—Does thyrotoxicosis have a specific stimulating effect on the heart aside from the over-activity of increased work?

Third—Does hyperthyroidism cause hypertrophy and dilatation of the normal heart from increased work, or from a specific stimulating effect, or both?

In consideration of the first question, if it can be demonstrated that myocardial injury results from thyrotoxicosis, it can be safely assumed that congestive heart failure will eventually result from prolonged intoxication. Wilson[1] has examined the hearts of 21 patients with hyperthyroidism, 18 of which showed marked lipoid changes. These patients fall in the age group where degenerative changes are frequently seen, so that, unless some specific pathological change due to thyroid toxicity is demonstrated, we must rely more on clinical observation to arrive at the probable answer to this question. Hamilton[2] has stated that, in his opinion, thyroid toxicity has a selective action on certain individual hearts. Since he does not specify what is characteristic of these individual hearts, this conclusion cannot be accepted until more definite clinical data have been presented. As to previous cardiac injury precipitating heart failure, we would expect in a community where rheumatic heart disease is prevalent many cases of failure in hyperthyroidism associated with mitral stenosis. Furthermore, as the age advances in which we find congestive heart failure, we should expect to find a considerable number with associated arteriosclerotic and hypertensive changes.

Concerning the second question, that of a specific stimulating effect of thyrotoxicosis on the heart aside from the increased work present, clinical observation supports this supposition. In many patients who have lost most signs of toxicity, and whose pulse and basal metabolic rates have returned to normal as the result of iodine administration

*From the Lahey Clinic, Boston, Mass.
Read before the American Heart Association at Minneapolis, June 12, 1928.

and rest, the characteristic thyroid thrust of the heart is often present far out of proportion to the then present demands of the circulation. The thyroid gland has undergone involution, the bruit disappears, the low diastolic pressure returns to normal limits, and still the thrust remains. As Willius and Boothby have pointed out[1] in other conditions where the basal metabolic rate is increased as in leucemia, or in moderate exercise, such as walking, the heart impulse is barely if at all palpable. This specific stimulation of the heart is, we believe, an important secondary factor in the production of cardiac failure.

In regard to the third question, Boas[3] believes that cardiac hypertrophy in hyperthyroidism is the result of increased oxygen demands and the increased flow through the thyroid gland. The latter he compares to an arterio-venous aneurysm or shunt. Read[4] believes that increased metabolic rate adds to the work of the heart and, if long continued, will result in myocardial failure. It is our impression, based on repeated teleroentgenograms—and others, I believe, are of the same opinion[1, 5]—that cardiac hypertrophy is rare in hyperthyroidism, except in a certain group of cases and in these it can usually be explained by coexistent cardiovascular disease. Our experience has been that the heart is too often considered enlarged because of the characteristic thrust and the movement of the thoracic cage. As a rule, the thyroid heart found in the patient dying of hyperthyroidism is flabby,[1, 6] and this impression is also gained by fluoroscopy. Such a condition would be consistent with some dilatation and we feel that the functional systolic murmurs so frequent in hyperthyroid hearts cannot adequately be explained on any other basis. Such dilatation and flabbiness are not characteristic of work hypertrophy, but is more consistent with the general muscular weakness which is so characteristic of thyroid over-activity.

CLINICAL DATA

Of the 500 cases of hyperthyroidism, 479 were of the exophthalmic type and 21 were of the toxic adenomatous type. The usual criteria were used in establishing the clinical diagnosis of hyperthyroidism and all cases studied showed confirmatory pathological changes in the gland removed at operation.

The criteria for diagnosis of cardiac changes were as follows:

1. Rheumatic heart disease with mitral stenosis was diagnosed only when a well-defined mitral diastolic murmur was evident.

2. Questionable rheumatic heart disease was diagnosed when there was a harsh apical systolic murmur, often a rheumatic history and usually some degree of enlargement.

3. Hypertension was diagnosed in the presence of a blood pressure of 190/90 mm. or more, or with a diastolic pressure of 100 mm. or more, regardless of the systolic pressure.

4. Arteriosclerosis was considered present when there was well-marked hypertrophy, tortuosity, and hardening of the peripheral vessels.

5. Luetic aortitis was diagnosed when an aortic regurgitant murmur was present along with a positive Wassermann. (The two cases included both had dilated aortic arches.)

6. Established auricular fibrillation was diagnosed when this irregularity remained present from the time of admission to the hospital until operation.

7. Paroxysmal auricular fibrillation occurred in most cases postoperatively, and was diagnosed only when personally observed.

8. Transient congestive heart failure. All patients having a clear-cut history of past failure relieved by rest and iodine before coming under our observation were placed in this group.

9. Paroxysmal tachycardia and auricular flutter were identified by the electrocardiogram.

10. True congestive heart failure. All of these patients had pitting edema of the legs, the neck veins were always distended in the upright position and the liver edge was down. Orthopnea of varying degrees was present. The degree of failure varied, of course, some clearing with rest and iodine, while others required the use of digitalis and diuretics.

TABLE I

CLASSIFICATION OF HEARTS IN 500 CASES OF HYPERTHYROIDISM

TYPE	NUMBER OF CASES	AVERAGE AGE IN YEARS	DURATION OF HYPERTHYROIDISM IN MONTHS
I. No change	339	35	17 mo.
II. Paroxysmal auric. fibrillation	20	49	12 mo.
With heart changes	20		
III. Probable rheumatic heart	14	27	13 mo.
With failure and auric. fibrillation	2	42	(7 mo.-8 yr.)
IV. Rheumatic heart	21	35	11 mo.
With failure and auric. fibrillation	2	50	11 mo.
V. Established auricular fibrillation	36	49	14 mo.
(3 hypertensive) (all types)	56	53	16 mo.
VI. Transient congestive failure			
Normal rhythm (4 hypert.)	13	42	7 mo.
With est. aur. fib. (1 hypert.)	3	57	8 mo.
VII. Hypertensive heart	24	54	18 mo.
With luetic aortitis	1		
VIII. Cardiac hypertrophy	4	60	10 mo.
? of cause—no failure			
IX. Angina pectoris (1 hypert.)	2		
X. Paroxysmal tachycardia	2		
XI. Auricular flutter	2		
XII. Congestive heart failure	26		
(a) Rheumatic	2	50	11 mo.
(b) ? Rheumatic	2	42	(7 mo.-8 yr.)
(c) Arteriosclerotic and hypertensive	13	54	28 mo.
(d) Luetic (included in above)	1		
(e) ? Cause	9	51	38 mo.*
Total C. H. F.	26	49	

*The duration in this group showed a mean of about 18 months; two patients dated their onset 8 and 12 years but in each case it was questionable.

DISCUSSION

There are certain very obvious facts to be noted from this tabulation. In the first place, the duration of the hyperthyroidism does not seem to play a consistent part in the production of auricular fibrillation, or of congestive heart failure. The basal metabolic rate varied considerably and showed no relation to the degree of congestive heart failure. No attempt was made to correlate the basal metabolic rates because of the frequent iodinization before coming under our observation.

Of importance we feel is the freedom from congestive heart failure in the group with mitral stenosis. On the assumption that previous myocardial damage is necessary to precipitate failure in hyperthyroidism, this finding is rather surprising. On the other hand, the average age of this group is the same as those cases which we considered as having no heart changes. This brings up the important point of age, which we will again emphasize as being a paramount factor in the production of congestive failure in hyperthyroidism.

The low average age of the questionable rheumatic heart group serves to confirm the clinical diagnosis which was made in these cases. Here again those showing failure were far above the average age of all the rheumatic cases.

It is interesting to note in regard to age that we find more heart disturbances (particularly established or paroxysmal fibrillation) as we approach fifty years. The average age of the established auricular fibrillation group was forty-nine, while in those showing congestive heart failure with this irregularity it was above fifty years. One-third of the total of 36 cases with hypertension showed frank congestive heart failure. Here again we note the factor of age, for the average age of this group is fifty-four years. Those patients showing well-marked arteriosclerosis had an average age of fifty-six years; of these patients four were males. If arteriosclerosis were more common in females, we feel that we would see a greater number of cases showing congestive heart failure. In the 26 cases of congestive heart failure 17 showed definite hypertensive or arteriosclerotic changes.

The remaining 9 cases in the congestive failure group, in so far as could be determined, showed no evidence or gave no history of coincident cardiovascular disease. These patients showed many features in common. Cardiac enlargement was present in most instances and by x-ray the enlargement was often shown to be both to left and right. Electrocardiograms showed no preponderance of either ventricle; low voltage was seen in half the cases and auricular fibrillation was present in the majority. Congestive failure was not of the extreme type, having been improved in all cases by rest, iodine, and (occasionally) digitalis.

Sufficient time to form a final opinion as to the end-results in all the congestive failure cases in this group has not elapsed, but previ-

ous experience gives us the impression that the prognosis in each case depends on the amount of coexisting cardiovascular disease present. Three of the failure group herein reported are dead. One died of pneumonia before operation, another died of congestive heart failure five months after operation, having had hypertensive and rheumatic heart disease, and a third died suddenly after four months of comparative freedom from cardiac disability.

CONCLUSIONS

From the data presented what conclusions can we draw in regard to the etiology of congestive heart failure in hyperthyroidism?

First, if thyrotoxicosis injures the normal healthy heart we believe there should be more evidence of injury below the age of forty. The average age of the congestive heart failure group being above fifty years, with a large percentage showing coexisting cardiovascular disease, leads us to conclude, on a clinical basis at least, that if there is a selective action of hyperthyroidism it chooses the heart in patients who are over forty years old. If auricular fibrillation is to be considered evidence of myocardial damage from thyrotoxicosis, it certainly should be present more often in the younger patient and particularly should it have a more definite relationship to duration and degree of toxicity.

The nine cases showing no clinical evidence of coexisting cardiovascular disease, present an important group in regard to the question of myocardial injury as the result of thyrotoxicosis. Because of the small number of patients and their advanced age we feel we cannot attribute their heart failure to thyrotoxicosis directly, but believe that these patients have some unrecognized myocardial weakness either from previous unknown injury or because they belong to that group of individuals who inherit a predisposition to cardiovascular degeneration. The drive of hyperthyroidism serves to bring out this inherited weakness, and although the average duration of the disease is somewhat longer in this group, this seems a natural explanation in view of the lack of gross clinical evidence of more advanced cardiovascular disease.

Second, we believe that thyrotoxicosis has a specific excitatory effect on the heart and that this, more than the increased work from circulatory demands, produces failure in a heart weakened by the degenerative processes of age.

Third, our clinical observation leads us to believe that hypertrophy of the heart does not take place in a normal healthy heart as the result of hyperthyroidism, but that dilatation is probably frequent. Duration, we feel, plays a very little part in a general way. It is obvious, however, from frequent examinations of thyroid patients that duration as well as degree of toxicity plays an important rôle in individual

cases. Immediate removal of thyroid toxicity by surgical procedure is undoubtedly the quickest and surest method of averting the onset of congestive heart failure.

Therefore, in conclusion, we consider the most significant causes of congestive heart failure in hyperthyroidism: (1) age and the coexisting cardiovascular changes associated with it; (2) the specific heart drive incited by thyrotoxicosis; (3) auricular fibrillation; (4) duration and intensity of thyroid overactivity.

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(*For discussion, see page* 116.)

THE DISTORTION OF THE ELECTROCARDIOGRAM BY CAPACITANCE*

A Critical Analysis of the Electrical Amplification of Heart Currents

William Dock, M.D.
San Francisco, Cal.

THE introduction of a condenser (electrical capacity or capacitance) in series with the leads from the patient to the string galvanometer has a well-known effect in distorting the electrocardiogram. The relations of this effect to polarization of electrodes, to skin changes in myxedema, and its use in obviating the need for a variable current to

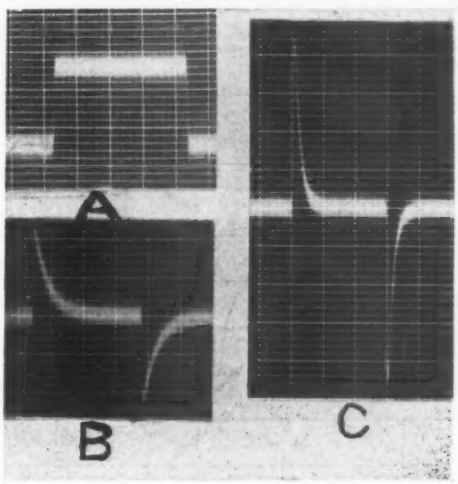
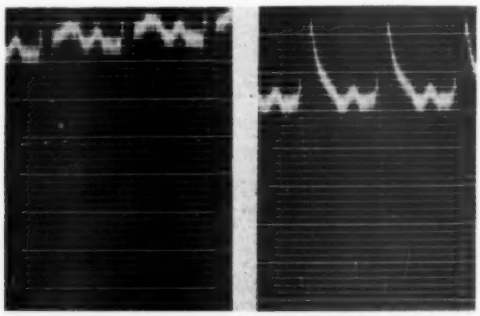


Fig. 1.—*A*. The normal make and break curve of the string galvanometer. External resistance 3200 ohms.
B. The same, with 20 microfarad capacity in the circuit, string returns one-half distance to zero in 0.07 seconds.
C. The same, external resistance reduced to 500 ohms, one-half decrement period reduced to 0.04 seconds. On the break, in *B* and *C*, the string moves in the opposite direction to the make.

neutralize skin currents are known to all who are familiar with electrocardiography. The recent introduction of resistance-and-capacitance-coupled amplifiers into electrocardiographic technic calls for a reconsideration of this distortion, as the only descriptions of these instruments[1, 2] give no critical data bearing on this point. Many of the users of these new instruments are more or less unfamiliar with this distortion and have made no extensive comparison of their instruments with the string galvanometer.

*From the Medical Clinic of the Stanford University Medical School, San Francisco.

A capacitance, introduced into an electrical circuit, impedes direct flow of current, but permits surge in the line. Fig. 1 shows the effect of a capacity on the curve due to make-and-break of a constant current applied to a string galvanometer. At the make the normal deflection occurs, but is not sustained; the return to the zero line occurs at a rate inversely proportional to the circuit resistance and to the size of the capacity. On the break, the string moves in the opposite direc-



A. *B.*

Fig. 2.—*A.* Normal curve (Lead III) of a person with left axis deviation.
B. The same, after introducing 20 microfarad capacity into circuit. Note shortened S-wave and distortion of S-T due to capacitance.

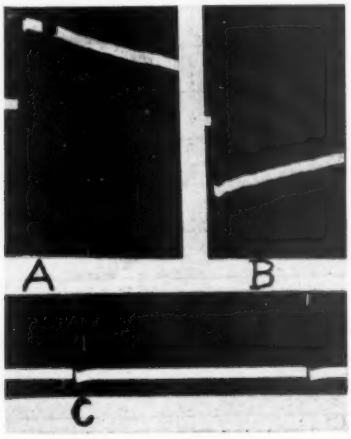


Fig. 3.—*A.* Make of 1 millivolt current (3200 ohms external resistance) as recorded by a three-tube amplifier electrocardiograph, period of one-half decrement is 1.35 sec.
B. Break of same current in same instrument.
C. Rapid make and break; note overshooting of base line even with current of short duration and one millivolt amplitude.

tion due to the surge in the line and again returns to the base line. In Fig. 2 the distortion of the electrocardiogram produced by a capacitance is clearly shown because the unusually large QRS deflection accentuates the effect. In Fig. 3 is shown the effect of make-and-break, and of a current of brief duration on the record made by a very good amplifier-type electrocardiograph. Control tests of make-and-

break with the galvanometer of this instrument showed curves similar to Fig. 1-*A*. It will be noted that the period needed for 50 per cent return to zero after make is twenty times as long as with the string galvanometer with a 20 microfarad capacitance. The latter shows but little distortion of normal tracings and is satisfactory and routinely used in this laboratory for experimental observations on small animals and birds. While the amplifier-type instrument is far more accurate than the combination just mentioned, it does distort an important part of the electrocardiogram, as shown by the overshooting past the zero line on "break" in Fig. 3, and by a comparison of the true (string galvanometer) curves with those recorded by this instrument on the same patient (Fig. 4). The terminal part of

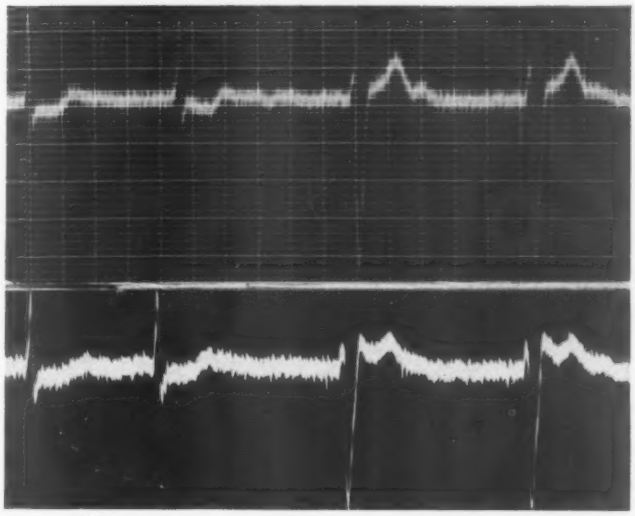


Fig. 4.—Upper curve, string galvanometer record. Lower, three-tube amplifier electrocardiograph record. Note the exaggerated S and flattened T of the first two beats, the marked S-T distortion of the last two beats.

the QRS and onset of T are distorted in the same way although to a less degree than in Fig. 2. To those who are interested, not merely in relation of events in the cardiac cycle, electrical axis deviation, and the like, but also in the details of the ventricular complex, the present amplifier-type electrocardiographs are therefore unsatisfactory. The ventricular complex distortion increases in proportion to the duration and voltage of the QRS deflection. It may conceal changes due to coronary disease, or produce distortion suggestive of such changes in patients whose QRS is of high voltage.

SUMMARY

Capacitance, introduced into the circuit with a string galvanometer or incorporated into an amplifier for heart currents, distorts the ven-

tricular complex. This distortion increases with decrease in resistance and capacitance in the circuit, and with increase in the voltage of the QRS deflection. Electrocardiographic tracings made with amplifier-type instruments can only duplicate accurate string galvanometer tracings when make-and-break test currents give records similar to those of the Einthoven electrocardiograph. The usual distortion of the QRS complex, due to capacitance in the amplifier, is slight but must be considered in reading the tracings produced by the instruments now available.

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THE USE OF FAHNESTOCK CLIPS IN THE TECHNIC OF TAKING ELECTROCARDIOGRAMS*

HAROLD J. STEWART, M.D.
NEW YORK, N. Y.

A YEAR ago, acting on the suggestion of Herrmann and Wilson[1] we began to use flexible copper wire as electrodes in taking electrocardiograms on patients in the clinic and on animals in the laboratory. We have found this electrode satisfactory both from the point of view of consistently obtaining low skin resistances and also because of ease of application. Herrmann and Wilson used double connecting binding posts to connect the lead wires to the copper wires. In the routine use of double binding posts we frequently found

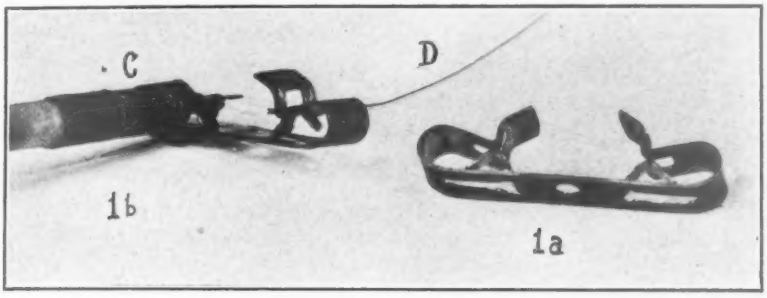

Fig. 1-a.—A photograph of a Fahnestock clip. 1-b, shows the lead wire (*C*) connected to one of the Fahnestock clips and copper wire (*D*) used as the electrode connected to the other end. One-half natural size.

that the screws of the binding posts were not adjusted tightly. This resulted in distortion of the electrocardiogram and waste of time in making readjustments. It occurred to us to substitute brass Fahnestock clips† (Fig. 1) for the double connecting binding posts. The spring clip automatically makes a tight connection. The adjustment is much quicker than the use of binding posts with screws. The clips can be left attached to the lead wires.

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*From The Hospital of the Rockefeller Institute for Medical Research, New York.

†Fahnestock clips have come into extensive use in wiring radio apparatus. They can be obtained for 5 to 10 cents per clip. They last indefinitely. If, from repeated use, the spring becomes pushed down too far so that the small guage wire does not fit tightly under the clip, the spring can be spread.

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Official Organ of the American Heart Association

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Coordination of Investigation

A COMMITTEE of the American Heart Association, known as the Committee for the Coordination of Investigation, was organized in October, 1927, for the purpose of fostering collective research in the more definitely medical and scientific aspects of heart disease, and has decided upon a definite program for research to occupy the coming year. The committee consists of seven members, Dr. Edward C. Carter of Baltimore, Dr. Cary Eggleston of New York, Dr. Edward B. Krumbhaar of Philadelphia, Dr. H. M. Marvin of New Haven, Dr. Paul D. White of Boston, Dr. Frank N. Wilson of Ann Arbor, and Dr. Harold E. B. Pardee of New York, who is the Chairman of the Committee.

A schema for the study of cardiovascular syphilis has been elaborated by this committee, and various interested workers throughout the country have been invited to take part in the study, thereby becoming contributing members of the committee. Up to the present time more than thirty men have signified their desire to take up one or more of the phases of this subject. With the cooperation of these numerous workers, it is confidently believed that this study should

result in a definite advance in our knowledge of the etiology, the pathology, the clinical diagnosis, and the treatment of syphilis of the heart and aorta.

The committee will be glad to increase the number of contributing members. Anyone wishing to take part in this investigation may make application to become a contributing member, and to do this should communicate with the chairman, outlining briefly the phase of the subject which he desires to cover. It is hardly possible to have too many investigators engaged in this work. No harm will be done, and probably much benefit will accrue, even if two or three men should be working on exactly the same problem. The agreement or the discrepancies in their findings might well be of much importance. The committee would be glad also to send to any one who is interested to receive it the schema which has been prepared, outlining the study of the subject as a whole. It is expected, not that any one person should investigate all the problems outlined in this schema, but that each man should select those which he is best fitted to attack, or those in which he has the greatest interest. The results of this investigation will be reported at the next annual meeting of the American Heart Association and will constitute the scientific session of this organization. It is hoped that the combined researches may be published in book form.

Society Transactions

AMERICAN HEART ASSOCIATION

FOURTH ANNUAL SCIENTIFIC SESSION

JUNE 12, 1928

The fourth annual scientific session of the American Heart Association was called to order shortly after two o'clock on Tuesday, June 12, 1928, in the Ball Room of the Leamington Hotel in Minneapolis, Minnesota, as follows:

The Chairman, DR. WILLIAM H. ROBEY, Boston, Mass.—Ladies and gentlemen, we have waited, I think, as long as we can for our president, Dr. James B. Herrick of Chicago, who was to begin the meeting. I am sorry there is not a larger attendance. Some of the speakers would like to have a lantern, and I believe that one is being brought from somewhere—I think in this city—so that the first paper I will call for is by Dr. Hurxthal.

1. DR. LEWIS M. HURXTHAL, Boston, Mass.—**Heart Failure and Hyperthyroidism.** (For original article see page 403.)

2. DR. ROBERT H. HALSEY, New York, N. Y.—**Observations on the Mortality of Heart Disease in New York State.** (For original article see page 94.)

3. DR. PAUL W. EMERSON, AND DR. HYMAN GREEN, Boston, Mass.—**Idiopathic Hypertrophy of the Heart in Infants.***

It would be better to designate the tremendous increase in the size of the heart described in the literature as "idiopathic hypertrophy" by the term, "hypertrophy of unknown etiology," but so few cases have been reported that for the present, to keep the literature on the subject accessible, we have retained the old name. Such enlarged hearts described by Howland in his classical article showed hypertrophy and nothing else except in two instances a very small open foramen ovale. He was of the opinion that it was unjustifiable to discard a case as one of idiopathic hypertrophy merely because it showed likewise a simple defect. The two kinds of cases, hypertrophy with simple defect and hypertrophy without, are so similar clinically that one might, before post-mortem examination of the heart, swear as to the correctness of a diagnosis, only to find that without a murmur, a simple defect such as a foramen ovale, an open interventricular septum or a patent ductus arteriosus would be present, or that with a murmur nothing would be shown except a hypertrophy.

We believe that such cases of idiopathic hypertrophy which also have simple defects are worthy of reporting as a class and we have five such cases. With the purpose of emphasizing this class we are reporting six cases of idiopathic hypertrophy of the heart without other defect. In all of the cases the hearts were enlarged to from two and a half to four times the normal size, and in all of them

*Abstract of paper read at the Fifth Annual Scientific Session of the American Heart Association in Minneapolis.

dyspnea and cyanosis were the most common symptoms. The oldest patient was twenty-eight months of age. Seven died within one week after admission to the hospital. We could find no satisfactory etiology for this disease but we suspect that a possible and as yet uninvestigated cause may be a congenital narrowing of the capillary bed. There were eight autopsies.

4. Dr. B. J. Clawson, Minneapolis, Minn.—**Fibrosis of the Myocardium.** (See Myocarditis, page 1.)

5. Dr. Robert L. Benson, Portland, Ore.—**Rupture of the Heart.**

DISCUSSION

The Chairman.—This has been a most interesting group of speeches that has been presented this afternoon, and I will ask Dr. Albert to open the discussion.

Dr. Henry Albert, Des Moines, Iowa.—Mr. Chairman. From the public health point of view, which is the point of view in which I am interested, it is very encouraging to note the very great interest which is being manifested in the study of heart disease, not only by the public and the medical profession in general, but also by special groups, such as is, for instance represented by this association. The public has become interested the past few years, largely because heart disease is now the leading cause of death in this country, and mortality from heart disease also is, and for some years has been, on the increase.

On the other hand, the public health official meets with two great difficulties when it comes to heart disease. *First.*—Heart disease is not a definite thing like tuberculosis and typhoid fever. Heart disease varies so widely in its nature and is produced by such diverse causes, that the problem of evaluating the influence or effect of the several factors is a very complex and difficult one. *Second.*—Heart disease does not present the urgent call for immediate attention that we have in connection with diphtheria or scarlet fever or other readily communicable diseases. When you have to wait ten or fifteen years after the cause started to act before the disease forces itself on your attention, you can readily appreciate that the busy health officer is much more likely to look after quarantinable diseases and the paying public is much more interested in having the health department protect them from dangers immediately at hand.

I was much interested this afternoon, especially in the reference made by Dr. Halsey of the importance of securing certain statistical data. He suggested that the cause of heart disease be included on the death certificate. Now, I agree with him that it is very desirable to have more definite data than we now get. We who are gathering statistics in state public health departments are interested in having as definite data as possible with reference to the cause of disease, but as far as heart disease is concerned, the cause is not susceptible of being given in as definite a form as in connection with most other conditions, and certainly it is not as simple as would be implied by simply dividing it into rheumatic, syphilitic, and arteriosclerotic groups. We may speak rather definitely with reference to the rheumatic and syphilitic forms but when it comes to arteriosclerosis, we have here to deal with a pathological condition, or possibly as suggested by some, with a normal senescent process—rather than an etiological factor. When it comes to a case of arteriosclerosis we have to deal with many factors, some of which are as yet but poorly understood.

A year or so ago I delved into a certain speculative field. I got the notion that more cases of heart disease were caused by scarlet fever than it had been given credit for. Once having decided upon that notion I wanted to get the data to

substantiate the notion, and on the general supposition that most cases of scarlet fever probably cause a certain amount of injury—some causing a chronic nephritis; others chronic heart disease; and others, milder conditions. I desired to get this information in the form of statistics. At the present time there are many more people who have survived an attack of scarlet fever, and presumably been injured by the toxin liberated by the streptococcus which causes scarlet fever, than there were some years ago. Whereas in 1906 the scarlet fever morbidity rate was 112 per 100,000 population, in 1926 the rate was 268. On the other hand, in spite of this increase, or at least apparent increase, in the number of cases, the mortality rate has decreased from six per 100,000 population in 1906 to two in 1926. According to this, then, there were, in 1906 one hundred and six persons out of every 100,000 population who survived an attack of scarlet fever that particular year, whereas in 1926 there were 266 persons that thus survived—an increase of 150 per cent. When we consider that this increase has occurred in a rather progressive way almost every year since 1906, it means that the cumulative effect has been very great. I noticed in last week's *Journal of the American Association* a reference to a contribution on allergy made by Dr. Swift. I don't know just how that process works, but I hope that Dr. Swift is right, largely from the standpoint of substantiating my theory. I hope he finds that a considerable number of cases of heart disease are due to scarlet fever.

It is apparent that the solution of the heart disease problem requires not only careful research as to etiology, pathology, diagnosis and treatment, but that it also requires some long range public health statesmanship. I know of no problem in medicine that is in greater need of effective cooperative work between the pathologist, the clinician, and the public health official.

DR. B. S. OPPENHEIMER, New York, N. Y.—Mr. Chairman, the paper of Dr. Emerson interested me because we have had a few such cases of hypertrophy of the heart in infants. We have no explanation to offer as to the cause. I recall one case. This was a boy born in 1920—certainly normal—and he died at the age of 19 months. About a week before he died he became very cyanotic. Attention was first attracted to the unusually large heart. Teleroentgenograms showed the huge heart he had. There were rapidly progressing symptoms of cardiac failure, from which he died. The autopsy revealed no pathological condition of the chest at all. The weight of the heart at 19 months was 125 grams. A normal heart for this age would be at most 50 grams. This weighed two and a half times as much as it should at that age. It was not a man's sized heart; it was the heart of a child of ten.

I should like to ask Dr. Emerson if there is any evidence that these cases live to adult life. As far as I know they have all been fatal. I should like to ask him, too, if it is possible that these cases may be due to the narrowing of the capillary bed, and whether that would explain the general hypertrophy of the heart.

I should like to speak for a moment also concerning Dr. Clawson's work. I think the difference between the statistics which Dr. Halsey presented and the figures from Dr. Clawson is accounted for by the fact that the doctors in the East call everything chronic myocarditis. Dr. Halsey's paper makes it clear that one should not apply the term myocarditis to myolysis. I think that distinction must be made in order to clear the question of diagnosis on death certificates.

DR. JOSEPH SAILER, Philadelphia, Pa.—Myocarditis is an unsatisfactory diagnosis. Our medical students are taught to diagnose it too readily. Usually if the pulse and the heart sounds are weak and the patient is old, it is assumed. As a rule it is difficult to obtain confirmation from the pathological department.

I wish I could agree with Dr. Oppenheimer that myocardial changes can be recognized in the electrocardiogram. I have met only one case in which the tracing was of proved value. The patient was an old woman, and we diagnosed before her death that there was a thrombus in one of the branches of the coronary artery. This was subsequently demonstrated by filling the coronary circulation with metallic mercury and taking an x-ray.

DR. HYMAN GREEN, Boston, Mass.—Idiopathic hypertrophy of the heart has been confused with other chest conditions. It has been diagnosed tuberculous effusion and mediastinal newgrowth. In two cases to our knowledge a needle has been inserted into the chest, and in one case through the heart itself for what was thought to be a pericardial effusion. These cases have been known to us only a short time, but we feel that with the increased knowledge of blood pressure, the electrocardiogram, and x-rays we will better be able to diagnose this condition. The electrocardiogram is not as yet an absolute means of making the diagnosis, however, the curves are fairly characteristic. Our cases all died of heart failure. Digitalis was tried in a few but was absolutely of no avail.

THE CHAIRMAN.—I have talked this matter over with Dr. Mallory, who assured me that acute inflammatory conditions of the heart muscle such as we get in rheumatism do the heart no material injury. It seems to me difficult to believe that you can have these minute scars in the heart without bringing on considerable trouble later in life, but I understood Dr. Clawson to say that it did not materially damage the heart, and other pathologists have insisted upon that also.

Is there any further discussion upon the papers we have listened to this afternoon? If there is none, I will entertain a motion to adjourn.

(Upon motion duly made and seconded the meeting adjourned.)

Department of Reviews and Abstracts

Selected Abstracts

Keefer, Chester S., and Resnik, William H.: Angina Pectoris. Arch. Int. Med., 1928, xli, 769.

In this paper the authors present a theory which explains the attacks of angina pectoris on a basis of localized anoxemia of the myocardium. They believe that the attack occurs when the oxygen supply to the heart is inadequate to meet the oxygen demands of the heart. In the usual case of angina, the anoxemia is relative, being sufficient for the needs of the heart at rest and insufficient when the work of the heart is increased. In acute coronary occlusion, however, the anoxemia is absolute, since the oxygen supply is inadequate, even when the heart is at rest.

Anoxemia of the myocardium may exist without causing angina. They point out that under these conditions when anoxemia affects all the tissues of the body as well as the heart, for example in pernicious anemia, or when the heart is uniformly affected so far as one may judge, angina is usually absent. When the heart is affected in such cases the symptoms are practically always those of so-called congestive heart failure.

On the other hand, angina tends to appear when in spite of anoxemia being present the contractural power of the heart remains good, evidenced by more or less complete freedom from dyspnea or other symptoms of a failing myocardium. These conditions occur most commonly when only a restricted part of the heart muscle suffers from lack of oxygen, as in coronary sclerosis. The remainder is relatively uninvolved and hence the contractural power of the heart remains good.

Parkinson, John, and Bedford, E. Evan.: Successive Changes in the Electrocardiogram After Cardiac Infarction (Coronary Thrombosis). Heart, xiv, 195.

Electrocardiograms are given from twenty-eight cases in which the diagnosis of cardiac infarction was made. Twenty-two patients are still alive and six have died; in four of the latter necropsies were obtained, each confirming the diagnosis.

The modifications of the ventricular complexes of the electrocardiogram following cardiac infarction are described in detail, and illustrated by serial records. Usually a definite sequence of changes in the R-T segment and in the T-waves is recorded. Shortly after the onset of symptoms a transient deviation of the R-T segment from the isoelectric plane occurs. This is followed by a deep inversion of the T-wave in either Lead I or Lead III, but not in both, and often by a lesser degree of T inversion in Lead II. Curves obtained after a few weeks conform to one of two main types according to the incidence of T inversion in Lead I or in Lead III. Subsequent T-wave changes in the direction of the normal are recorded, and even complete return to normal occurs. A negative T-wave in Lead III alone may be significant of past infarction.

T-wave changes seen in clinical curves are comparable with those observed

in experimental curves after coronary ligation, or after focal injury to the myocardium. The significance of modifications of the R-T segment and of the T-waves is discussed. The definite train of events seen in the electrocardiogram can be correlated with the pathological changes evoked in the myocardium by coronary occlusion. The R-T deviation indicates active spread of the area of necrosis. It is suggested that T-wave inversion indicates impairment of myocardial function in the area of distribution of the occluded artery, and that such impairment of function is not confined to the limits of the actual necrosis. The return of the T-waves toward normal corresponds to a progressive recovery of function of the myocardium in the territory of the occluded vessel. Such functional improvement can be explained by the development of a compensatory collateral circulation, by the increased circulatory efficiency and rise of blood pressure after recovery from shock and by the subsidence of edema and cellular exudation around the infarct.

Hume, W. E.: The Action of Adrenalin Chloride on the Human Heart. Quart. Jour. Med., 1928, xxi, 459.

The general effects of intravenous injections of small amounts of adrenalin chloride are considered. The electrocardiographic records are described from three individuals into whom a similar injection had been made and the effects of adrenalin chloride on the mechanism of the heart have been recorded. Two of the cases developed ectopic ventricular beats in regular repetition. One of the three cases showed transient auricular fibrillation.

Grant, R. T., and Jones, T. Duckett: A Case of Obstruction to the Cardiac Coronary Sinus. Heart, 1928, xiv, 241.

A case is recorded as an example of anatomical obstruction to the coronary circulation not on the arterial but on the venous side. The coronary sinus is occluded by a fibrous diaphragm apparently not due to a congenital malformation but to an old thrombus.

It would be thought that an obstruction in this situation if it did not cause death would interfere seriously with the coronary circulation but in the available history there is no unusual feature to suggest this nor was there any evidence in the heart itself of the impaired nutrition in the area drained by the occluded vein.

Grant, R. T., Wood, J. Edwin, Jr., and Jones, T. Duckett: Heart Valve Irregularities in Relation to Subacute Bacterial Endocarditis. Heart, 1928, xiv, 247.

From the point of view that subacute bacterial endocarditis arises through lodgement of bacteria on the valve surface a series of eighty-six hearts have been examined to note the irregularities present on the valves and to consider their possible relation to valvular infection.

The irregularities of the valve surface may be classified into two groups namely: recessions and projections. It is shown that neither recesses in the form of pockets and crevices nor projections in the form of connective tissue thickenings covered with endothelium can be regarded as offering bacteria a foothold on the valve.

It is found that small platelet thrombi occur with greatest frequency on those valves especially liable to subacute bacterial endocarditis. These thrombi are not themselves the result of bacterial invasion but are probably due to local secondary change in the thickened valves.

Such thrombi can be regarded as offering passing organisms a suitable foothold and nidus for their establishment.

It is suggested that if streptococcal invasion of the blood stream occurs at a time when a thrombus is forming on a heart valve then the conditions are suitable for the development of subacute bacterial endocarditis.

Kugel, M. A., and Epstein, Emanuel Z.: Lesions in the Pulmonary Artery and Valve Associated with Rheumatic Cardiac Disease. Arch. Path., 1928, vi, 247.

The present study was undertaken to determine the frequency and type of inflammatory changes in the pulmonary artery and valve and the adjacent fibrous ring in cases of rheumatic heart disease.

A systemmatical study was made in 24 cases of active rheumatic infection of the heart. In 5 of these histological examinations of the artery revealed an active inflammatory change consisting on the one hand of diffuse cellular infiltration in the intima and subintimal layers of the media and, on the other of a focal perivascular collection of cells comparable to the Aschoff nodules in the myocardium. These changes were similar to those described by Pappenheimer and von Glahn in the aorta. In two instances the intimal changes were sufficiently widespread to produce small macroscopic lesions on the inner surface of the vessel. In two cases the disruption of the elastic media was almost as conspicuous as in syphilis.

In fourteen of the active cases, the pulmonary valve was the seat of an interstitial valvulitis which involved a part of the whole of the valve, and in three of these the diffuse reactions was accompanied by the Aschoff bodies in the substance of the valve. Verrucae were present in six cases, but these were inconspicuous in all but two.

The musculo-arterial junction was the seat of active inflammation in seventeen of the twenty-four cases, or in 70.9 per cent. The more frequent type of reaction was of the diffuse variety, but Aschoff bodies were also present in a few.

In a comparative study of the aorta, its root and valves, the fibrous ring of this vessel which corresponds to the musculo-arterial junction of the pulmonary artery, was involved in twenty-two, or 90.7 per cent, of the twenty-four cases of active rheumatic heart disease. In four instances there were gross lesions in the intima, and these were more extensive in the aorta than in the pulmonary artery. Diffuse inflammatory changes were found in the wall of the artery in each of these cases. Aschoff bodies were not seen.

As controls, thirty-one cases of nonrheumatic pericarditis and seventy-five cases in which neither pericarditis nor rheumatic cardiac disease was present were studied. In one of the control cases lesions were found which could be confused with those seen in the pulmonary artery, valve and musculo-arterial junction in cases of active rheumatic cardiac disease.

Zinsser, Hans, and Yu, H.: The Bacteriology of Rheumatic Fever and the Allergic Hypothesis. Arch. Int. Med., 1928, lxii, 301.

The authors reported the cases described in this paper because they seemed to them to illustrate certain features in the bacteriology of rheumatic fever which were inconsistent with the assumption of a specific and single bacteriologic etiology in this disease. The cases were all of more or less the same clinical group; the organisms antigenically and in other respects differed from each other.

Moreover, the isolation of the bacteria in one case from the myocardium and in two—which illustrate the more chronic type of the disease—from the spleen, seems to offer a reasonable explanation for the frequent absence of these organisms from the blood stream and to point to the probable localization of the bacteria during the prolonged periods of quiescence. This also indicates the places

from which cultures at autopsy may be expected to yield the streptococci when they are absent from the blood and the pericardial exudate.

Moreover, a coordination of the observations in their cases with prolonged experimental studies on bacterial allergy seemed to them to lend added support to the point of view that focal infection with a consequent sensitization of the body is in keeping with the many otherwise contradictory experimental and clinical observations that have been made on this disease, and to lend added weight to the view that the allergic theory is a reasonable one as applied to the causation of many of the manifestations of rheumatic fever.

The authors have not yet been able in their experimental work to produce joint lesions in allergic animals except by direct injection of the antigen into the joints. All attempts to arouse sterile joint reactions in either allergic rabbits or guinea pigs by injecting the antigen intravenously or intraperitoneally have so far failed although they have been attempting this for a number of years. They have found that success in producing joint manifestations of any severity has usually necessitated repeated injections of the same joints.

The experimental circle of evidence, therefore, is not entirely closed, but it may be that in man the frequent association of joint manifestations with chilling, exposure, etc., may be due to the establishment thereby of abnormal circulatory communication between joints and the blood stream, in which sensitizing contact between the constituents of the blood stream and the joints can take place in a focally infected allergic person.

It seemed to them possible that the curious frequency with which nonhemolytic streptococci are associated with the disease, while at the same time nonhemolytic streptococci so found represent many varieties, may be due to the fact that with these organisms that peculiar balance between invasiveness and resistance is established in man, which most easily results in chronic infection.

At the same time, in appraising the significance of the different varieties of organism which Swift and his coworkers, as well as the authors, have found in one and the same case, it must be remembered that studies on bacterial mutation are considerably altering our opinions concerning the fixity of species; and modifications of the organisms inhabiting the body for months and years must be considered as possibilities until this chapter of bacteriology has made further progress.

The suggestion that many of the manifestations of rheumatic fever are dependent on the mechanism of bacterial hypersensitiveness is not a new one, but has been gaining force. On the whole, their observations of the last four or five years, both in the experimental study of bacterial allergy and in the analysis of clinical material, incline them to favor this view rather than that favored by Small, Birkhaug and others in which a single specific toxinforming organism is held responsible.

Kurtz, Chester M., and White, Paul D.: The Percussion of the Heart Borders and the Roentgen Ray Shadow of the Heart. A Study of One Hundred Cases. Amer. Jour. Med. Sc., 1928, clxxvi, 181.

The present paper is an endeavor to determine the trustworthiness of the percussion of the heart borders as compared with the "7 foot roentgen-ray plate."

The study is based on the examination of one hundred patients of all ages and both sexes seen in the out-patient department and wards of the Massachusetts General Hospital. The actual percussion was carefully done by three well trained observers and the roentgen-ray plates were measured and checked by a fourth.

Percussion is reasonably accurate as shown by comparison with a 7 foot roentgen-ray plate. It is simple, rapid and requires no apparatus and it is occasionally a valuable check on the accuracy of roentgen-ray technic and interpretation.

Percussion is of value in determining the cardiac outline especially in the third left interspace as this may be the only portion of the heart which is enlarged to physical examination, as in mitral stenosis and congenital heart disease. Percussion in the second interspace both to right and left and in the fourth right interspace should always be attempted because in case of marked increase widening can usually be detected even though the measurements themselves are bound to be inexact.

Hitchcock, C. H.: Studies on Indifferent Streptococci. 1. Separation of a Serological Group—Type I. Jour. Exp. Med., 1928, xlviii, 393.

Serological study of one hundred and fifty-nine strains of indifferent streptococci has revealed the existence of a large homogeneous group to which the designation Type I has been applied. All strains of Type I ferment inulin and salicin. The members of this type are not necessarily identical and further division into subtypes may be feasible.

Those strains not falling into the group of Type I are referred to as belonging to Group X. They are distinguished only by their failure to react strongly with Type I serum. The organisms of this group vary in their fermentive reactions with both inulin and salicin.

The organisms were secured from the throats of patients suffering from various diseases including rheumatic fever, from the throats of normal individuals, from the interior of tonsils removed at operation or from blood cultures of patients with acute rheumatic fever.

Hitchcock, C. H.: Studies on Indifferent Streptococci. II. Observations on the Distribution of Indifferent Streptococci in the Throats of Rheumatic and Non-Rheumatic Individuals. Jour. Exp. Med., 1928, xlviii, 403.

Indifferent streptococci occur in comparatively the same abundance in the throats of patients suffering from rheumatic fever or early in convalescence from the disease as they do in those who have recovered from the disease or in those of patients suffering from other diseases.

There is a slightly increased incidence of these microorganisms in the throats of hospital patients as compared with those of normal individuals.

Type I occurs with comparatively equal frequency and abundance in the throats of all four classes of individuals studied.

Cannell, D. E.: Myocardial Degenerations in Yellow Fever. Am. Jour. Path., 1928, iv, 431.

The microscopic examination and analysis of the hearts of twenty-nine cases of West African yellow fever and those of nine monkeys experimentally infected with West African yellow fever, is reported.

Cloudy swelling, granular and fatty degeneration were found constantly in the hearts of both the human cases and those experimentally induced in the monkeys.

Primary inflammatory changes were not seen in the hearts examined. Secondary response of white blood cells to intense degeneration was observed in two human cases.

The distribution and intensity of granular and fatty degeneration was patchy and variable. The lesions in the heart are in themselves not sufficient to make a diagnosis of yellow fever.

The causation of the slow pulse in yellow fever is still uncertain and doubt is thrown upon the belief that it is due to the jaundice.

Further investigation of the clinical function and the pathological changes in the bundle of His may lead to solution of this problem.

Johnson, Scott, and Siebert, Walter J.: Experimental Myocarditic Lesions in the Rabbit. Arch. Path., 1928, vi, 54.

The purpose of this study was to determine whether the heart of the rabbit in which myocarditis has been produced by the injection of caffeine and epinephrine is more susceptible to bacterial infection than the normal heart of the rabbit.

When rabbits so treated are subsequently injected intravenously with the bouillon culture of a suitable strain of staphylococcus aureus, abscesses of the heart are produced much more frequently than in rabbits not previously injected with caffeine and epinephrine. If a more active strain of staphylococcus is used, the abscesses occur even in the majority of the control animals. With this strain, also, the experimentally produced myocarditic lesion still influences the localization of the abscesses which develop in and around the myocarditic area mainly in the left ventricle and in the papillary muscles, and less frequently in the endocardium and in the left auricle.

Cardiac decompensation may be produced in rabbits by injection of caffeine and epinephrine alone as a result of the myocarditis thus produced; but the frequency of cardiac decompensation may be increased by subsequent injections of a suitable strain of staphylococcus aureus.

The proliferation of the endothelium which occurs adjacent to the myocardial lesion, following the injections of caffeine and epinephrine, appears to predispose the site of this lesion to the formation of mural thrombi in case a comparatively nonvirulent strain of staphylococcus aureus culture is injected into the blood stream subsequent to the injection of caffeine and epinephrine.

It was not possible to demonstrate any direct relationship between the acute vegetations on the valves of the heart and a lesion of the valves produced by the injections of caffeine and epinephrine.

The presence of a myocarditic lesion may indirectly favor the production of a fibrinous pericarditis and of pneumonia. On the other hand, injections of caffeine and epinephrine and the lesions produced thereby apparently do not markedly lower the resistance of the pericardium to the action of bacteria injected into the pericardial sac.

Bourne, C. R.: Auricular Flutter Restored to Normal Rhythm by Quinidine. Can. Med. Assn. Jour., 1928, xix, 180.

The interest in this report lies in the type of disturbance of cardiac mechanism and the method of its restoration to normal.

In a patient aged 38 there was an established auricular flutter in a heart definitely enlarged without gross cardiac failure. There was marked tolerance for quinidine and massive dosage was required to restore the normal mechanism of the heartbeat.

Digitalis improved the ventricular action, but apparently had a mild effect on the disappearance of the flutter.

Nathanson, M. H.: The Electrocardiogram in Diphtheria. Arch. Int. Med., 1928, xlii, 23.

In fifteen severe and moderately severe cases of diphtheria, approximately fifty per cent of the patients showed inversion of the T-wave in significant leads during convalescence.

Two patients showing inversion of the T-wave died suddenly.

In the patients that recovered, the inverted T-wave returned to normal as early as seven weeks after the onset of the disease.

Cats injected with sublethal doses of diphtheria toxin showed consistently similar T-wave alterations, usually within forty-eight hours.

These observations support the myocardial theory of the circulatory failure in diphtheria.

Barker, M. Herbert, and Levine, Samuel A.: Cardiazol: Some Experimental Effects of this Drug on the Cardiorespiratory Mechanism. Arch. Int. Med., 1928, xlii, 14.

In a series of experiments on cats it was found that cardiazol did not have any beneficial effect on the cardiorespiratory mechanism. This was true in the normal animal and in states of depression, produced by quinidine, hemorrhage and acid intoxication.

Miller, H. R., and Weiss, Morris M.: Disease of the Coronary Arteries. Arch. Int. Med., 1928, xlii, 74.

In cases of marked disease of the coronary vessels, together with a diseased heart on gross examination, the heart was found to be unhypertrophied and even small as revealed at autopsy in the nineteen cases tabulated in this study.

There were two patients with disease of the coronary arteries in whom clinical manifestations and roentgen-ray evidence pointed to cardiac enlargement. These hearts were dilated; they should not mistakenly be considered hypertrophied.

It may be that in the patients with disease of the coronary arteries in whom the heart remained small the organ failed to hypertrophy because it possessed a potential mechanism ready to function through adequate collateral channels whenever the coronary circulation was gradually blocked or impeded.

Carr, James H., and Reddick, Walter G.: Conduction Disturbances in Acute Rheumatic Infections. Jour. Am. Med. Assn., 1928, xci, 853.

This study covers fourteen cases of acute arthritis in which there was some disturbance of auriculo-ventricular conduction. This disturbance consisted of simple prolongation, incomplete block and complete block. The block was at times temporary.

In this group eight patients were taking sodium salicylate at the time the block was discovered and in no case was the drug stopped and in all the normal conduction time was restored while the same dosage was continued.